EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L2	1	"6670399".pn.	US-PGPUB; USPAT	OR	ON	2007/07/19 08:18
L3	5	"505268".ap.	US-PGPUB; USPAT	OR	ON	2007/07/19 08:18
S1	5	"505257".ap.	US-PGPUB; USPAT	OR	ON	2007/07/19 08:11
S2	5	"977609".ap.	US-PGPUB; USPAT	OR	ON	2006/11/20 07:16
S3	4	("5677282"|"5728650"|"5830869"|"6437165").PN.	US-PGPUB; USPAT	OR	ON	2007/01/26 14:54
S4	1	"6437165".PN.	US-PGPUB; USPAT	OR	ON	2007/01/29 07:39
S5	751	514/398.ccls.	US-PGPUB; USPAT	OR	ON	2007/01/29 07:08
S6	296	548/316.4.ccls.	US-PGPUB; USPAT	OR	ON	2007/01/29 07:08
S7	34	S5 and S6	US-PGPUB; USPAT	OR	ON	2007/01/29 07:09
S8	335	548/263.2	US-PGPUB; USPAT	OR	ON	2007/01/29 07:09
S9	482	514/389.ccls.	US-PGPUB; USPAT	OR	ON	2007/01/29 07:09
S10	5	S8 and S9	US-PGPUB; USPAT	OR	ON	2007/01/29 07:10
S11	623	548/255	US-PGPUB; USPAT	OR	ON	2007/01/29 07:10
S12	691	548/255.ccls.	US-PGPUB; USPAT	OR	ON	2007/01/29 07:10
S13	367	514/384.ccls.	US-PGPUB; USPAT	OR	ON	2007/01/29 07:11
S14	95	S8 and S13	US-PGPUB; USPAT	OR	ON	2007/01/29 07:11
S15	30	S12 and S13	US-PGPUB; USPAT	OR	ON	2007/01/29 07:11
S16	751	514/398.ccls.	US-PGPUB; USPAT	OR	ON	2007/01/29 07:11
S17	296	548/316.4.ccls.	US-PGPUB; USPAT	OR	ON	2007/01/29 07:12
S18	34	S16 and S17	US-PGPUB; USPAT	OR	ON	2007/01/29 07:12
S19	337	514/382.ccls.	US-PGPUB; USPAT	OR	ON	2007/01/29 07:13

Application Number	Application/Control No.	Applicant(s)/Patent under Reexamination	
	10/505,257	BUDHU ET AL.	
	Examiner	Art Unit	
	Yong Chu	1626	

EAST Search History

S20	542	548/251.ccls.	US-PGPUB; USPAT	OR	ON	2007/01/29 07:13
S21	43	S19 and S20	US-PGPUB; USPAT	OR	ON	2007/01/29 07:13
S22	330	558/169.ccls.	US-PGPUB; USPAT	OR	ON	2007/01/29 07:39
S23	793	514/114.ccls.	US-PGPUB; USPAT	OR	ON	2007/01/29 07:40
S24	126	558/70.ccls.	US-PGPUB; USPAT	OR	ON	2007/01/29 07:40
S25	65	558/116.ccls.	US-PGPUB; USPAT	OR	ON	2007/01/29 07:41
S26	0	S7 and S22	US-PGPUB; USPAT	OR	ON	2007/01/29 07:41
S27	39	S23 and S22	US-PGPUB; USPAT	OR	ON	2007/01/29 07:41
S28	0	S23 and S22 and S24	US-PGPUB; USPAT	OR	ON	2007/01/29 07:42
S29	0	S27 and S25	US-PGPUB; USPAT	OR	ON	2007/01/29 07:42

50/58 ODP Not ODP.
51/58 instat app.

10/505,257K Yong Chu 07-18-2007

$%^STN;HighlightOn=;HighlightOff=;

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:ssptaylc1626

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page for STN Seminar Schedule - N. America
NEWS 2	MAR 15	WPIDS/WPIX enhanced with new FRAGHITSTR display format
NEWS 3	MAR 16	CASREACT coverage extended
NEWS 4	MAR 20	MARPAT now updated daily
NEWS 5	MAR 22	LWPI reloaded
NEWS 6	MAR 30	RDISCLOSURE reloaded with enhancements
NEWS 7	APR 02	JICST-EPLUS removed from database clusters and STN
NEWS 8	APR 30	GENBANK reloaded and enhanced with Genome Project ID field
NEWS 9	APR 30	CHEMCATS enhanced with 1.2 million new records
NEWS 10	APR 30	CA/CAplus enhanced with 1870-1889 U.S. patent records
NEWS 11	APR 30	INPADOC replaced by INPADOCDB on STN
NEWS 12	MAY 01	New CAS web site launched
NEWS 13	MAY 08	CA/CAplus Indian patent publication number format defined
NEWS 14	MAY 14	RDISCLOSURE on STN Easy enhanced with new search and display fields
NEWS 15	MAY 21	BIOSIS reloaded and enhanced with archival data
NEWS 16	MAY 21	TOXCENTER enhanced with BIOSIS reload
NEWS 17	MAY 21	CA/CAplus enhanced with additional kind codes for German patents
NEWS 18	MAY 22	CA/CAplus enhanced with IPC reclassification in Japanese patents
NEWS 19	JUN 27	CA/CAplus enhanced with pre-1967 CAS Registry Numbers
NEWS 20	JUN 29	STN Viewer now available
NEWS 21	JUN 29	STN Express, Version 8.2, now available
NEWS 22	JUL 02	LEMBASE coverage updated
NEWS 23	JUL 02	LMEDLINE coverage updated
NEWS 24	JUL 02	SCISEARCH enhanced with complete author names
NEWS 25	JUL 02	CHEMCATS accession numbers revised
NEWS 26	JUL 02	CA/CAplus enhanced with utility model patents from China
NEWS 27	JUL 16	CAplus enhanced with French and German abstracts
NEWS 28	JUL 18	CA/CAplus patent coverage enhanced

NEWS EXPRESS 29 JUNE 2007: CURRENT WINDOWS VERSION IS V8.2,
CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 05 JULY 2007.

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8

G1:O,CH

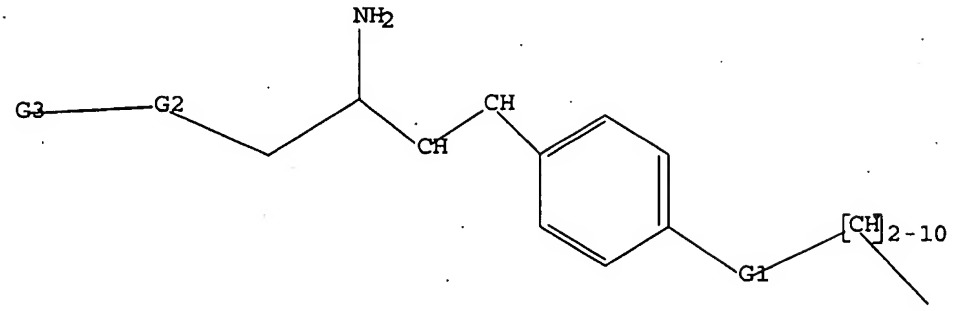
G2:C,N,O

G3:CO2H,PO3H2,SO2,SO3H,Hy

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS
11:CLASS 12:CLASS 16:CLASS 17:CLASS 19:CLASS 20:CLASS

L7 STRUCTURE UPLOADED

=> d
L7 HAS NO ANSWERS
L7 STR



G1 O,CH
G2 C,N,O
G3 CO2H,PO3H2,SO2,SO3H,Hy

Structure attributes must be viewed using STN Express query preparation.

=> s l7
SAMPLE SEARCH INITIATED 07:25:16 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 755 TO ITERATE

100.0% PROCESSED 755 ITERATIONS 4 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 13452 TO 16748
PROJECTED ANSWERS: 4 TO 200

L8 4 SEA SSS SAM L7

=> s l7 full
FULL SEARCH INITIATED 07:25:25 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 14458 TO ITERATE

100.0% PROCESSED 14458 ITERATIONS 103 ANSWERS
SEARCH TIME: 00.00.01

L9 103 SEA SSS FUL L7

=> file caplus
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 172.10 355.63

FILE 'CAPLUS' ENTERED AT 07:25:31 ON 19 JUL 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 19 Jul 2007 VOL 147 ISS 4
FILE LAST UPDATED: 18 Jul 2007 (20070718/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/infopolicy.html

=> s l9
L10 58 L9

=> d ibib abs hitstr tot

L10 ANSWER 1 OF 58 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:673023 CAPLUS Full-text
TITLE: Preparation of 2-amino-4-phenylbutanol and 2-amino-4-phenyl-3-buten-1-ol derivatives and their phosphate esters as immunosuppressants
INVENTOR(S): Kiuchi, Masatoshi; Marukawa, Kaoru; Kobayashi, Nobutaka; Sugahara, Kunio
PATENT ASSIGNEE(S): Mitsubishi Pharma Corporation, Japan
SOURCE: PCT Int. Appl., 152pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007069712	A1	20070621	WO 2006-JP325016	20061215

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN,

for the treatment of cancer

INVENTOR(S): Baumruker, Thomas; Brinkmann, Volker; La Montagne, Kenneth Richard; Lassota, Peter T.; Mechtcheriakova, Diana; Wood, Jeanette Marjorie

PATENT ASSIGNEE(S): Novartis AG, Switz.; Novartis Pharma GMBH

SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003097028	A1	20031127	WO 2003-EP5125	20030515
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SE, SG, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW				
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR				
CA 2483594	A1	20031127	CA 2003-2483594	20030515
AU 2003240655	A1	20031202	AU 2003-240655	20030515
EP 1505959	A1	20050216	EP 2003-730049	20030515
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003011173	A	20050315	BR 2003-11173	20030515
CN 1652757	A	20050810	CN 2003-811194	20030515
JP 2005529921	T	20051006	JP 2004-505027	20030515
ZA 2004008575	A	20050530	ZA 2004-8575	20041022
MX 2004PA11384	A	20050214	MX 2004-PA11384	20041116
NO 2004005312	A	20041203	NO 2004-5312	20041203
US 2005215531	A1	20050929	US 2005-513804	20050415
PRIORITY APPLN. INFO.:			GB 2002-11261 A	20020516
			US 2002-390411P P	20020620
			GB 2002-17150 A	20020724
			US 2003-449739P P	20030224
			WO 2003-EP5125 W	20030515

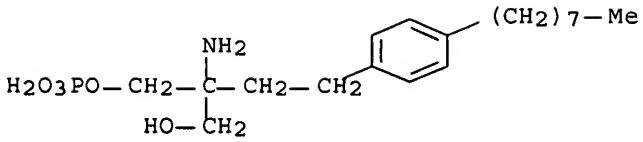
OTHER SOURCE(S): MARPAT 140:714

AB A method is disclosed for treating solid tumors, e.g. tumor invasiveness, and particularly inhibiting or controlling deregulated angiogenesis, using a sphingosine-1-phosphate (S1P) receptor agonist, optionally in combination with a chemotherapeutic agent. The invention also discloses a combination of a S1P receptor agonist with a chemotherapeutic agent.

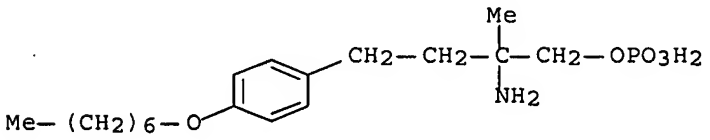
IT 402615-91-2 627809-68-1
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sphingosine-1-phosphate receptor agonists for treatment of cancer, and use with other agents)

RN 402615-91-2 CAPLUS

CN 1,3-Propanediol, 2-amino-2-[2-(4-octylphenyl)ethyl]-, 1-(dihydrogen phosphate) (CA INDEX NAME)



RN 627809-68-1 CAPLUS
CN Benzenebutanol, .beta.-amino-4-(heptyloxy)-.beta.-methyl-, dihydrogen phosphate (ester) (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 48 OF 58 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:896782 CAPLUS Full-text
DOCUMENT NUMBER: 140:139415
TITLE: Phosphorylation and Action of the Immunomodulator FTY720 Inhibits Vascular Endothelial Cell Growth Factor-induced Vascular Permeability
AUTHOR(S): Sanchez, Teresa; Estrada-Hernandez, Tatiana; Paik, Ji-Hye; Wu, Ming-Tao; Venkataraman, Krishnan; Brinkmann, Volker; Claffey, Kevin; Hla, Timothy
CORPORATE SOURCE: Department of Transplantation and Immunology, Farmington, University of Connecticut Health Center, Department of Cell Biology, Center for Vascular Biology, Novartis Institutes for BioMedical Research, Basel, 06030-3501, Switz.
SOURCE: Journal of Biological Chemistry (2003), 278(47), 47281-47290
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

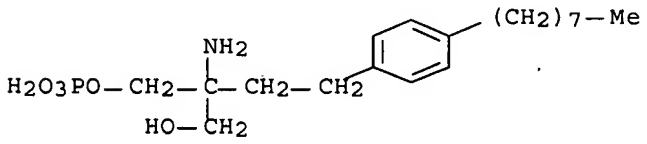
AB FTY720, a potent immunosuppressive agent, is phosphorylated in vivo into FTY720-P, a high affinity agonist for sphingosine 1-phosphate (S1P) receptors. The effects of FTY720 on vascular cells, a major target of S1P action, have not been addressed. We now report the metabolic activation of FTY720 by sphingosine kinase-2 and potent activation of vascular endothelial cell functions in vitro and in vivo by phosphorylated FTY720 (FTY720-P). Incubation of endothelial cells with FTY720 resulted in phosphorylation by sphingosine kinase activity and formation of FTY720-P. Sphingosine kinase-2 effectively phosphorylated FTY720 in the human embryonic kidney 293T heterologous expression system. FTY720-P treatment of endothelial cells stimulated extracellular signal-activated kinase and Akt phosphorylation and adherens junction assembly and promoted cell survival. The effects of FTY720-

P were inhibited by pertussis toxin, suggesting the requirement for Gi-coupled S1P receptors. Indeed, transmonolayer permeability induced by vascular endothelial cell growth factor was potently reversed by FTY720-P. Furthermore, oral FTY720 administration in mice potently blocked VEGF-induced vascular permeability in vivo. These findings suggest that FTY720 or its analogs may find utility in the therapeutic regulation of vascular permeability, an important process in angiogenesis, inflammation, and pathol. conditions such as sepsis, hypoxia, and solid tumor growth.

IT 402615-91-2
RL: BSU (Biological study, unclassified); BIOL (Biological study) (phosphorylation and action of immunomodulator FTY720 inhibits vascular endothelial cell growth factor-induced vascular permeability)

RN 402615-91-2 CAPLUS

CN 1,3-Propanediol, 2-amino-2-[2-(4-octylphenyl)ethyl]-, 1-(dihydrogen phosphate) (CA INDEX NAME)

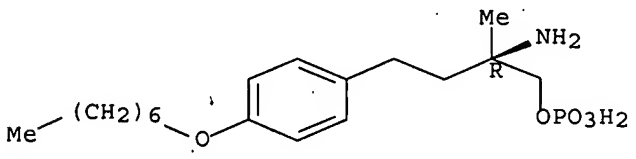


IT 479201-16-6
RL: BSU (Biological study, unclassified); BIOL (Biological study) (phosphorylation of (R)-ALL into (R)-AFD by sphingosine kinases in endothelial cells; phosphorylation and action of immunomodulator FTY720 inhibits vascular endothelial cell growth factor-induced vascular permeability)

RN 479201-16-6 CAPLUS

CN Benzenebutanol, .beta.-amino-4-(heptyloxy)-.beta.-methyl-, dihydrogen phosphate (ester), (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 49 OF 58 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:778468 CAPLUS Full-text
DOCUMENT NUMBER: 139:259937
TITLE: Rapid induction of medullary thymocyte phenotypic maturation and egress inhibition by nanomolar sphingosine 1-phosphate receptor agonist
AUTHOR(S): Rosen, Hugh; Alfonso, Christopher; Surh, Charles D.; McHeyzer-Williams, Michael G.
CORPORATE SOURCE: Department of Immunology, The Scripps Research

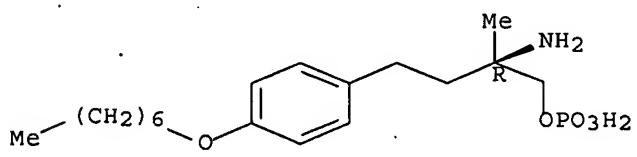
Institute, La Jolla, CA, 92037, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2003), 100(19), 10907-10912
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Only a small no. of T cells generated in the thymus each day are selected to replenish the peripheral T cell pool. Much is known about thymic selection; however, little is known of the mechanisms regulating medullary maturation and the release of mature T cells into the blood. Here the authors demonstrate a rapid acceleration of medullary thymocyte phenotypic maturation through loss of CD69 induced by sphingosine 1-phosphate (S1P) receptor agonist. Low nanomolar agonist concns. selectively induce changes in CD69int CD62Lhigh single pos. T cells, resulting in down-modulation of CD69 within 2 h. While CD69 loss is accelerated, egress of mature T cells into blood is inhibited >95% within 2 h. Both processes exhibit parallel sensitivities and dose-responses. Together, these data reveal a potent means for rapidly regulating thymic export where S1P receptor agonism alters both phenotypic maturation and egress of thymocytes into blood during late thymic maturation. The S1P system is now shown to acutely regulate both thymic and lymph node egress. Inhibition of lymphocyte egress from thymus and lymph node can contribute synergistically to clin. useful immunosuppression by disrupting recirculation of peripheral T cells.

IT 479201-16-6
RL: BSU (Biological study, unclassified); PKT (Pharmacokinetics); BIOL (Biological study)
(rapid induction of medullary thymocyte phenotypic maturation and egress inhibition by nanomolar sphingosine 1-phosphate receptor agonist)

RN 479201-16-6 CAPLUS
CN Benzenebutanol, .beta.-amino-4-(heptyloxy)-.beta.-methyl-, dihydrogen phosphate (ester), (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 66 THERE ARE 66 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 50 OF 58 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:719274 CAPLUS Full-text
DOCUMENT NUMBER: 139:246116
TITLE: Preparation of aminoalkylphosphonates and related compounds as EDG receptor agonists
INVENTOR(S): Doherty, George A.; Hale, Jeffrey J.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003074008	A2	20030912	WO 2003-US7262	20030225
WO 2003074008	A3	20040226		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2477449	A1	20030912	CA 2003-2477449	20030225
AU 2003218056	A1	20030916	AU 2003-218056	20030225
EP 1482896	A2	20041208	EP 2003-714037	20030225
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2005107345	A1	20050519	US 2003-505268	20030225
JP 2005531508	T	20051020	JP 2003-572530	20030225
PRIORITY APPLN. INFO.:			US 2002-360605P	P 20020301
			WO 2003-US7262	W 20030225

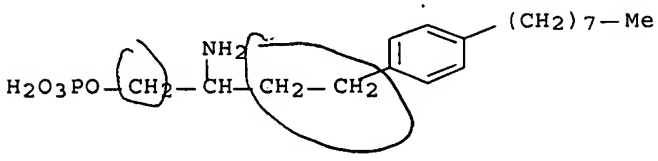
OTHER SOURCE(S): MARPAT 139:246116

AB The present invention encompasses title compds., A-X[CR1R2]mCHNH2[CR3R4]pC(R9)3 (m = 1-4; p = 9-20; X = bond, O, NH, S(O)k, k = 0-2; A = CO2H, PO3H2, PO2H2, SO3H, five membered nitrogen contg. heterocyclyl, etc.; two R1 or R3 groups on adjacent carbon may be joined together to form a double bond; R2, R3, R4 = H, halo, OH, CO2H, C1-4 alkyl, alkoxy, alkylthio, aryl, etc.; R1-R4 = residing on the same carbon optionally joined together to form a carbonyl group, etc.; R9 = H, halo, OH, C1-4 alkoxy, alkylthio, C3-7 cycloalkyl, etc.); as well as the pharmaceutically acceptable salts and hydrates thereof. The compds. are useful for treating immune mediated diseases and conditions, such as bone marrow, organ and tissue transplant rejection. Pharmaceutical compns. and methods of use are included. Thus, prepn. of (+/-)-2-amino-4-(4- (octylphenyl))butanol, O-phosphate was described in five steps starting from di-Et 2-acetamido-2-(2-(4-octylphenyl)ethyl)propanedioate.

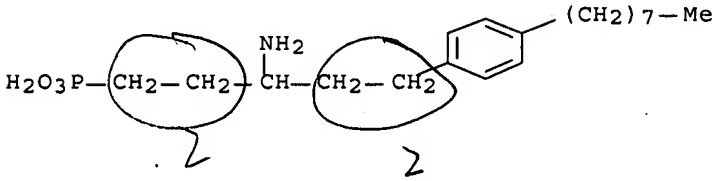
IT 596819-80-6P 596819-84-0P 596819-85-1P
596819-88-4P 596819-89-5P 596819-90-8P
596819-92-0P 596819-94-2P 596819-95-3P
596819-96-4P 596819-97-5P 596819-99-7P
596820-00-7P 596820-06-3P 596820-07-4P
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of aminoalkylphosphonates and related compds. as EDG receptor agonists)

RN 596819-80-6 CAPLUS

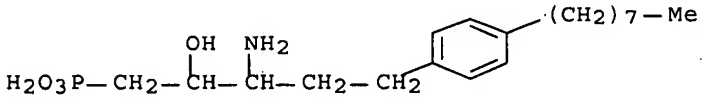
CN Benzenebutanol, .beta.-amino-4-octyl-, dihydrogen phosphate (ester) (9CI) (CA INDEX NAME)



RN 596819-84-0 CAPLUS
CN Phosphonic acid, [3-amino-5-(4-octylphenyl)pentyl]- (9CI) (CA INDEX NAME)



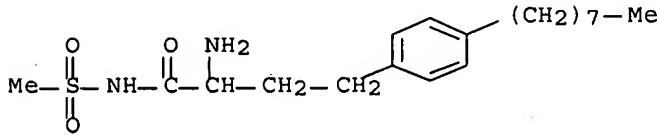
RN 596819-85-1 CAPLUS
CN Pentitol, 3-amino-1,2,3,5-tetradeoxy-1-(4-octylphenyl)-5-phosphono- (9CI) (CA INDEX NAME)



RN 596819-88-4 CAPLUS
CN Benzenebutanamide, .alpha.-amino-N-(methylsulfonyl)-4-octyl-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

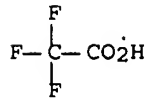
CM 1

CRN 596819-87-3
CMF C19 H32 N2 O3 S

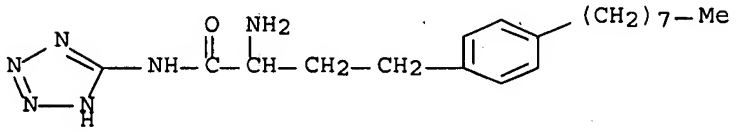


CM 2

CRN 76-05-1
CMF C2 H F3 O2

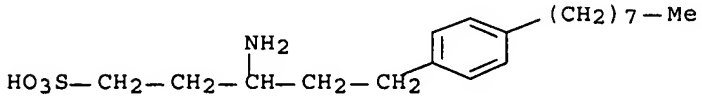


RN 596819-89-5 CAPLUS
CN Benzenebutanamide, .alpha.-amino-4-octyl-N-1H-tetrazol-5-yl-, monohydrochloride (9CI) (CA INDEX NAME)

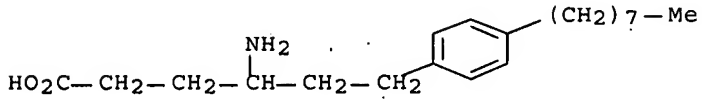


● HCl

RN 596819-90-8 CAPLUS
CN Benzenepentanesulfonic acid, .gamma.-amino-4-octyl- (9CI) (CA INDEX NAME)



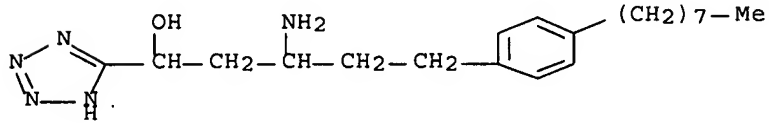
RN 596819-92-0 CAPLUS
CN Benzenehexanoic acid, .gamma.-amino-4-octyl- (9CI) (CA INDEX NAME)



RN 596819-94-2 CAPLUS
CN 1H-Tetrazole-5-methanol, .alpha.-[2-amino-4-(4-octylphenyl)butyl]-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

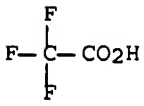
CM 1

CRN 596819-93-1
CMF C20 H33 N5 O



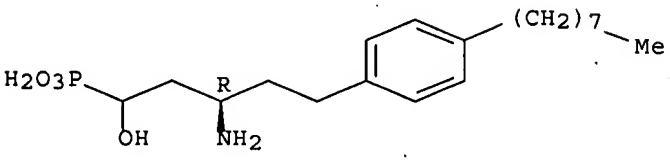
CM 2

CRN 76-05-1
CMF C2 H F3 O2



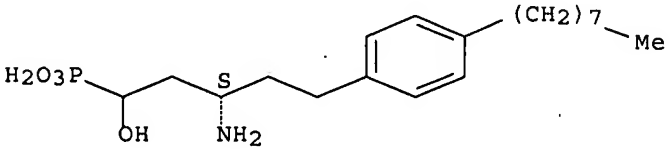
RN 596819-95-3 CAPLUS
CN Phosphonic acid, [(3R)-3-amino-1-hydroxy-5-(4-octylphenyl)pentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



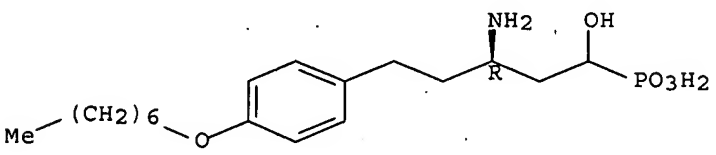
RN 596819-96-4 CAPLUS
CN Phosphonic acid, [(3S)-3-amino-1-hydroxy-5-(4-octylphenyl)pentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 596819-97-5 CAPLUS
CN Phosphonic acid, [(3R)-3-amino-5-[4-(heptyloxy)phenyl]-1-hydroxypentyl]- (9CI) (CA INDEX NAME)

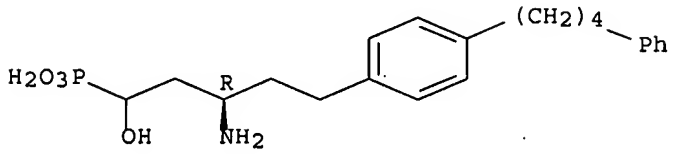
Absolute stereochemistry.



RN 596819-99-7 CAPLUS
CN Phosphonic acid, [(3R)-3-amino-1-hydroxy-5-[4-(4-

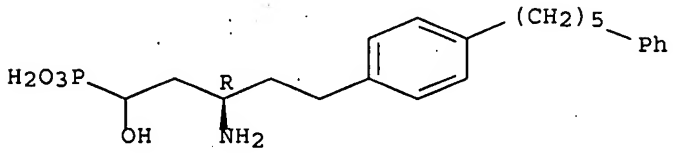
phenylbutyl)phenyl]pentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



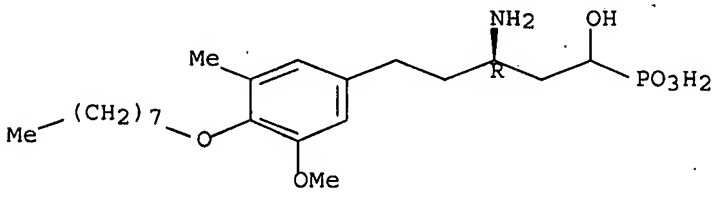
RN 596820-00-7 CAPLUS
CN Phosphonic acid, [(3R)-3-amino-1-hydroxy-5-[4-(5-phenylpentyl)phenyl]pentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



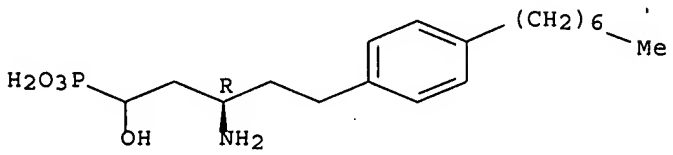
RN 596820-06-3 CAPLUS
CN Phosphonic acid, [(3R)-3-amino-1-hydroxy-5-[3-methoxy-5-methyl-4-(octyloxy)phenyl]pentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 596820-07-4 CAPLUS
CN Phosphonic acid, [(3R)-3-amino-5-(4-heptylphenyl)-1-hydroxypentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



instant app

L10 ANSWER 51 OF 58 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:719253 CAPLUS Full-text
DOCUMENT NUMBER: 139:245479
TITLE: Preparation of aminoalkylphosphonates and related compounds as EDG receptor agonists
INVENTOR(S): Budhu, Richard J.; Doherty, George A.; Hale, Jeffrey J.; Lynch, Christopher L.; Mills, Sander G.; Neway, William E., III
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 90 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003073986	A2	20030912	WO 2003-US5947		20030227
WO 2003073986	A3	20040527			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2477423	A1	20030912	CA 2003-2477423		20030227
AU 2003217764	A1	20030916	AU 2003-217764		20030227
EP 1482895	A2	20041208	EP 2003-713727		20030227
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
JP 2005531506	T	20051020	JP 2003-572508		20030227
US 2006089334	A1	20060427	US 2004-505257		20040819
PRIORITY APPLN. INFO.:			US 2002-360663P	P	20020301
			WO 2003-US5947	W	20030227

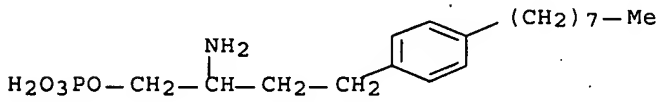
OTHER SOURCE(S): MARPAT 139:245479

AB AX(CR1R2)mCH(NH2)(CR3R4)nArBC [A = CO2H, P(O)(OH)2, PH(O)(OH), SO3H, P(O)R5OH, 5-membered N heterocycle; X = bond, O, NH, S, S, S(O), SO2; R1-R4 = H, halogen, OH, CO2H, (un)substituted alkyl, alkoxy, alkylthio, aryl; R1R2, R3R4 = O; m = 1-4; n = 0-4; R5 = (un)substituted alkyl, aryl; Ar = Ph, naphthyl; C = (un)substituted alkyl, alkoxy, acyl, hydroxyalkyl, Ph, heterocyclic, bond; when C = bond, B = (un)substituted Ph, alkyl, alkenyl, alkynyl, OH, SH, acyl, CONH2, NH2; when C = Ph, heterocyclic, B = (un)substituted alkyl, alkoxy, acyl, CO, CH(OH), C6H4, heterocyclic; when C = alkyl, alkoxy, acyl, B = (un)substituted C6H4, heterocyclic] were prepd. for use as EDG receptor antagonists useful for treating immune mediated diseases and conditions, such as bone marrow, organ and tissue transplant rejection (no data). Thus, 4-Me(CH2)7C6H4CH2CH2C(NHAc)(CO2Et)2 was hydrolyzed and decarboxylated to 4-Me(CH2)7C6H4CH2CH2CH(NH2)CO2H which was N-benzyloxycarbonylated, reduced to 4-Me(CH2)7C6H4CH2CH2CH(NHCbz)CH2OH , phosphorylated (MeCH)2NP(OCH2Ph)2, and deblocked to give 4-Me(CH2)7C6H4CH2CH2CH(NH2)CH2OP(O)(OH)2.

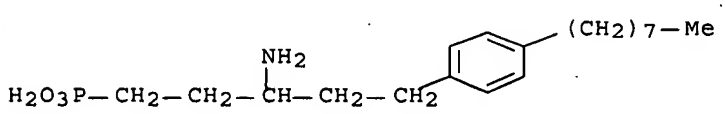
IT 596819-80-6P 596819-84-0P 596819-85-1P
596819-88-4P 596819-89-5P 596819-90-8P
596819-92-0P 596819-97-5P 596819-99-7P

596820-00-7P 596820-06-3P 596820-07-4P
597340-06-2P 597340-13-1P 597340-18-6P
597340-22-2P 597340-27-7P 597340-33-5P
597342-93-3P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of aminoalkylphosphonates and related compds. as EDG receptor agonists)

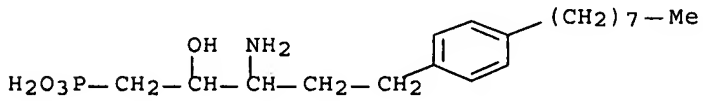
RN 596819-80-6 CAPLUS
CN Benzenebutanol, .beta.-amino-4-octyl-, dihydrogen phosphate (ester) (9CI) (CA INDEX NAME)



RN 596819-84-0 CAPLUS
CN Phosphonic acid, [3-amino-5-(4-octylphenyl)pentyl]- (9CI) (CA INDEX NAME)



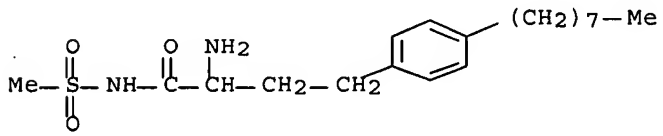
RN 596819-85-1 CAPLUS
CN Pentitol, 3-amino-1,2,3,5-tetradeoxy-1-(4-octylphenyl)-5-phosphono- (9CI) (CA INDEX NAME)



RN 596819-88-4 CAPLUS
CN Benzenebutanamide, .alpha.-amino-N-(methylsulfonyl)-4-octyl-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

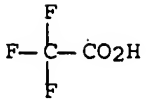
CM 1

CRN 596819-87-3
CMF C19 H32 N2 O3 S

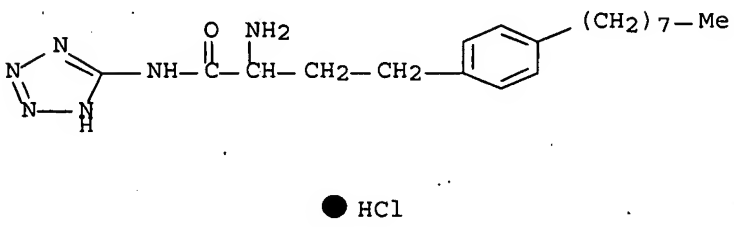


CM 2

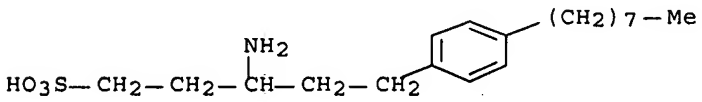
CRN 76-05-1
CMF C2 H F3 O2



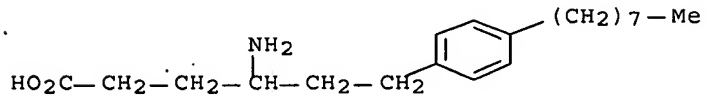
RN 596819-89-5 CAPLUS
CN Benzenebutanamide, .alpha.-amino-4-octyl-N-1H-tetrazol-5-yl-, monohydrochloride (9CI) (CA INDEX NAME)



RN 596819-90-8 CAPLUS
CN Benzenepentanesulfonic acid, .gamma.-amino-4-octyl- (9CI) (CA INDEX NAME)

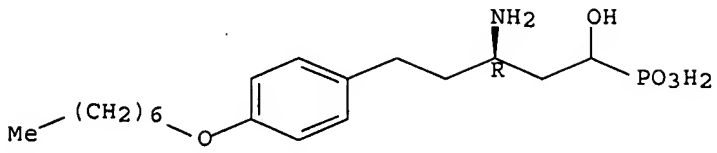


RN 596819-92-0 CAPLUS
CN Benzenehexanoic acid, .gamma.-amino-4-octyl- (9CI) (CA INDEX NAME)



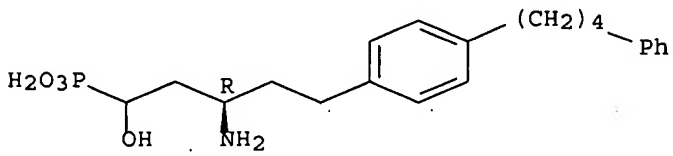
RN 596819-97-5 CAPLUS
CN Phosphonic acid, [(3R)-3-amino-5-[4-(heptyloxy)phenyl]-1-hydroxypentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



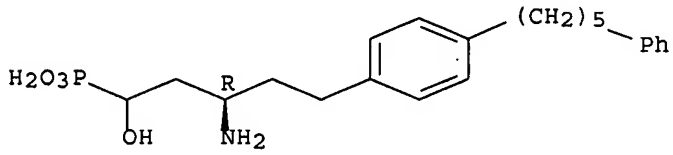
RN 596819-99-7 CAPLUS
CN Phosphonic acid, [(3R)-3-amino-1-hydroxy-5-[4-(4-phenylbutyl)phenyl]pentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



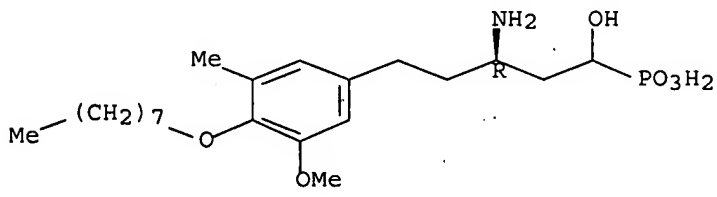
RN 596820-00-7 CAPLUS
CN Phosphonic acid, [(3R)-3-amino-1-hydroxy-5-[4-(5-phenylpentyl)phenyl]pentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



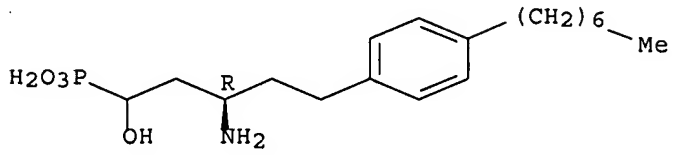
RN 596820-06-3 CAPLUS
CN Phosphonic acid, [(3R)-3-amino-1-hydroxy-5-[3-methoxy-5-methyl-4-(octyloxy)phenyl]pentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 596820-07-4 CAPLUS
CN Phosphonic acid, [(3R)-3-amino-5-(4-heptylphenyl)-1-hydroxypentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

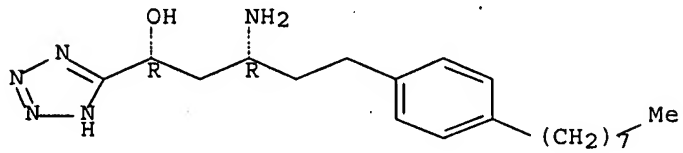


RN 597340-06-2 CAPLUS
CN 1H-Tetrazole-5-methanol, .alpha.-[(2R)-2-amino-4-(4-octylphenyl)butyl]-, (.alpha.R)-rel-, trifluoroacetate (salt) (9CI) (CA INDEX NAME)

CM 1

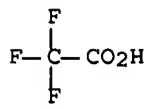
CRN 597340-05-1
CMF C20 H33 N5 O

Relative stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

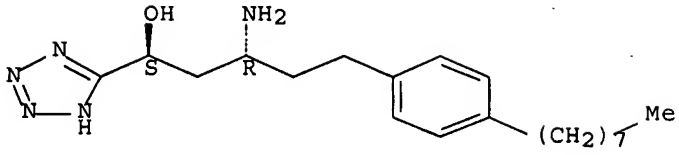


RN 597340-13-1 CAPLUS
CN 1H-Tetrazole-5-methanol, .alpha.-[(2R)-2-amino-4-(4-octylphenyl)butyl]-, (.alpha.S)-rel-, trifluoroacetate (salt) (9CI) (CA INDEX NAME)

CM 1

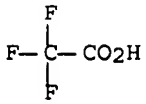
CRN 597340-12-0
CMF C20 H33 N5 O

Relative stereochemistry.



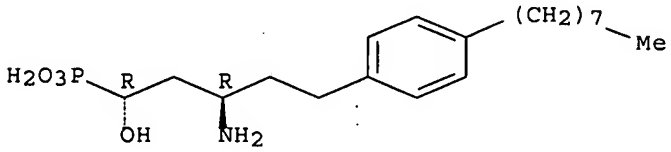
CM 2

CRN 76-05-1
CMF C2 H F3 O2



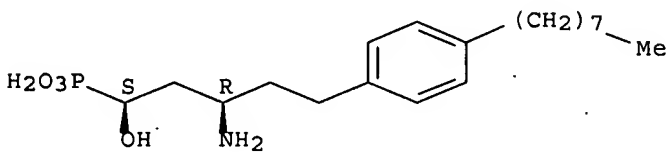
RN 597340-18-6 CAPLUS
CN Phosphonic acid, [(1R,3R)-3-amino-1-hydroxy-5-(4-octylphenyl)pentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



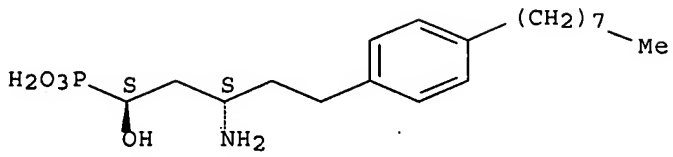
RN 597340-22-2 CAPLUS
CN Phosphonic acid, [(1S,3R)-3-amino-1-hydroxy-5-(4-octylphenyl)pentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



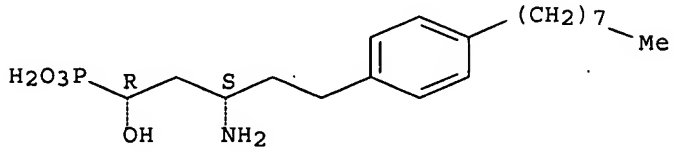
RN 597340-27-7 CAPLUS
CN Phosphonic acid, [(1S,3S)-3-amino-1-hydroxy-5-(4-octylphenyl)pentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

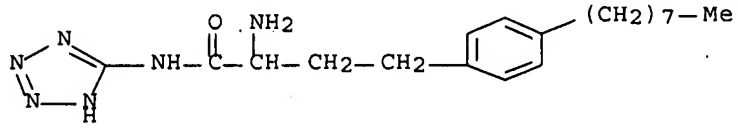


RN 597340-33-5 CAPLUS
CN Phosphonic acid, [(1R,3S)-3-amino-1-hydroxy-5-(4-octylphenyl)pentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 597342-93-3 CAPLUS
CN Benzenebutanamide, .alpha.-amino-4-octyl-N-1H-tetrazol-5-yl- (9CI) (CA INDEX NAME)



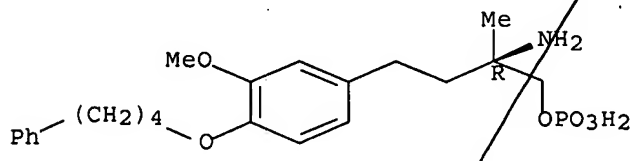
L10 ANSWER 52 OF 58 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:651906 CAPLUS Full-text
DOCUMENT NUMBER: 140:42245
TITLE: Synthesis of chiral analogues of FTY720 and its phosphate
AUTHOR(S): Hinterding, Klaus; Cottens, Sylvain; Albert, Rainer; Zecri, Frederic; Buehlmayer, Peter; Spanka, Carsten; Brinkmann, Volker; Nussbaumer, Peter; Ettmayer, Peter; Hoegenauer, Klemens; Gray, Nathanael; Pan, Shifeng
CORPORATE SOURCE: Novartis Institutes for Biomedical Research, Basel, 4002, Switz.
SOURCE: Synthesis (2003), (11), 1667-1670
CODEN: SYNTBF; ISSN: 0039-7881
PUBLISHER: Georg Thieme Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 140:42245

AB Efficient and versatile protocols for the synthesis of chiral analogs of the novel immunomodulator FTY720 [i.e., 2-amino-2-[2-(4-octylphenyl)ethyl]- 1,3-propanediol hydrochloride] and its phosphate are described. These synthetic procedures allow for broad structural variation and deliver essential tools to further elucidate FTY720's novel mechanism of action. Analogs of FTY720 thus prepd. included (2S)-2-amino-2-[2-[(4- heptyloxy)phenyl]ethyl]-4-pentyn-1-ol, phosphoric acid mono-[(2S)-2-amino-2-[2-[(4-heptyloxy)phenyl]ethyl]-4-pentynyl] ester, (2R)-2-amino-4-[3-methoxy-4-(4-phenylbutoxy)phenyl]-2-methyl-1-butanol, (2R)-2-amino-2-ethyl-4-[3-methoxy-4-(4-phenylbutoxy)phenyl]-2-methyl-1- butanol, phosphoric acid mono-[(2S)-2-amino-2-[2-[(4-heptyloxy)phenyl]ethyl]-5-hydroxypentyl] ester.

IT 463951-99-7P 463952-00-3P 463952-07-0P
634893-21-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of chiral analogs of FTY720 and its phosphate)

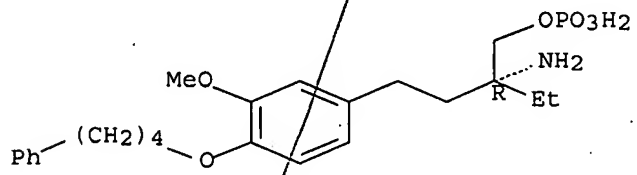
RN 463951-99-7 CAPLUS
CN Benzenebutanol, .beta.-amino-3-methoxy-.beta.-methyl-4-(4-phenylbutoxy)-, dihydrogen phosphate (ester), (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



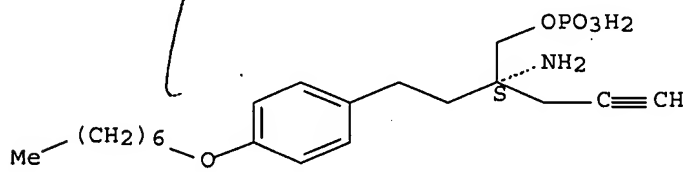
RN 463952-00-3 CAPLUS
CN Benzenebutanol, .beta.-amino-.beta.-ethyl-3-methoxy-4-(4-phenylbutoxy)-, dihydrogen phosphate (ester), (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



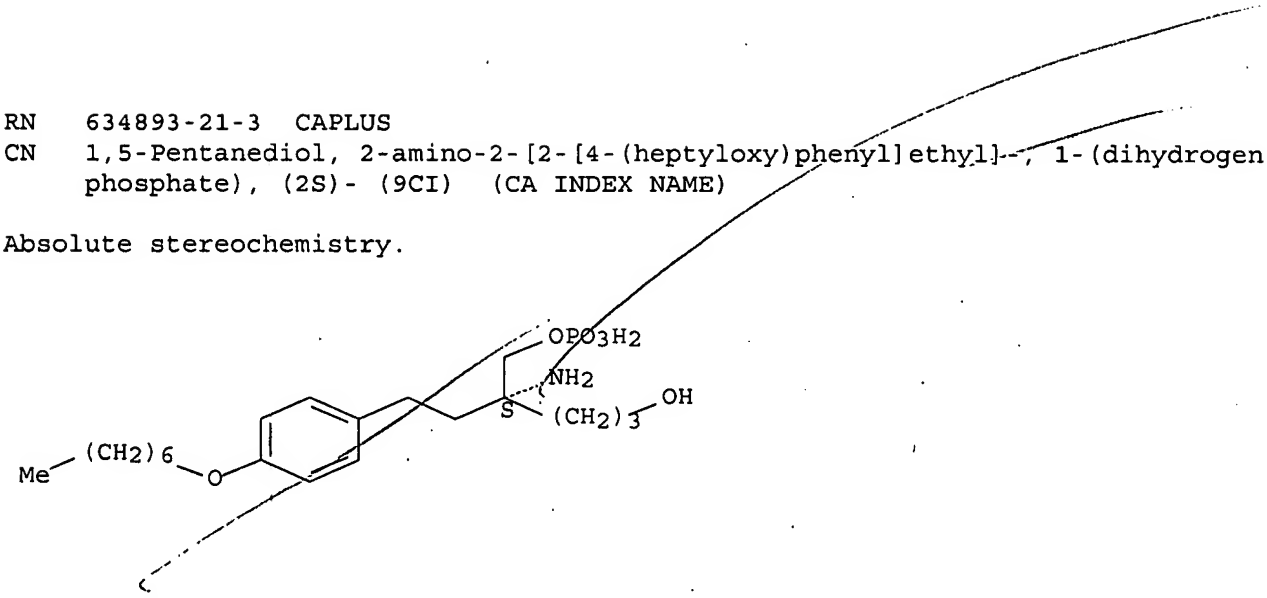
RN 463952-07-0 CAPLUS
CN Benzenebutanol, .beta.-amino-4-(heptyloxy)-.beta.-2-propynyl-, dihydrogen phosphate (ester), (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 634893-21-3 CAPLUS
CN 1,5-Pentanediol, 2-amino-2-[2-[4-(heptyloxy)phenyl]ethyl]-, 1-(dihydrogen phosphate), (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 53 OF 58 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:788570 CAPLUS Full-text
DOCUMENT NUMBER: 138:221031
TITLE: First asymmetric synthesis of chiral analogues of the novel immunosuppressant FTY720
AUTHOR(S): Hinterding, Klaus; Albert, Rainer; Cottens, Sylvain
CORPORATE SOURCE: Transplantation Research, Novartis Pharma AG, Basel, CH-4002, Switz.
SOURCE: Tetrahedron Letters (2002), 43(45), 8095-8097
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:221031

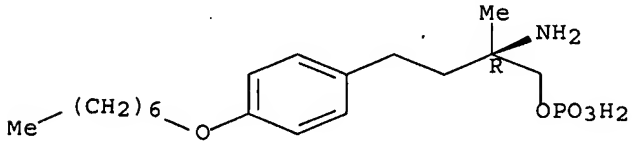
AP 11/4/2002

AB FTY720 is an immunosuppressant with a novel mode of action and is highly effective in animal models of transplantation and autoimmunity. Herein we describe the first asym. synthesis of chiral FTY720 analogs using the Schollkopf-protocol. We also describe a practical synthesis of the corresponding phosphates, which are essential tools for elucidation of FTY720's mechanism of action.

IT 479201-16-6P 479201-17-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of FTY720 analogs from D-cyclo-Val-Gly-OEt utilizing the Schollkopf-protocol)

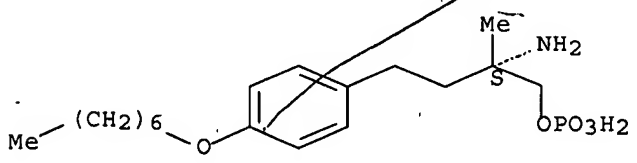
RN 479201-16-6 CAPLUS
CN Benzenebutanol, .beta.-amino-4-(heptyloxy)-.beta.-methyl-, dihydrogen phosphate (ester), (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 479201-17-7 CAPLUS
CN Benzenebutanol, .beta.-amino-4-(heptyloxy)-.beta.-methyl-, dihydrogen phosphate (ester), (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

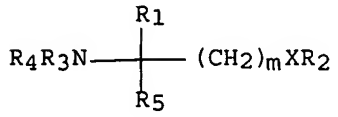
L10 ANSWER 54 OF 58 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:754397 CAPLUS Full-text
DOCUMENT NUMBER: 137:263181
TITLE: Preparation of 2-amino-propanol derivatives and their use in the treatment of diseases mediated by T lymphocytes
INVENTOR(S): Albert, Rainer; Baumruker, Thomas; Brinkmann, Volker; Cottens, Sylvain; Papageorgiou, Christos; Prieschl-Strassmayr, Eva Erika; Hinterding, Klaus
PATENT ASSIGNEE(S): Novartis Ag, Switz.; Novartis-Erfindungen Verwaltungsgesellschaft M.B.H.
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002076995	A2	20021003	WO 2002-EP3389	20020326
WO 2002076995	A3	20030213		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NO, NZ, OM, PH, PL, PT, RO, RU, SE, SG, SI, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VN, YU, ZA, ZW				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
CA 2442178	A1	20021003	CA 2002-2442178	20020326
AU 2002257719	A1	20021008	AU 2002-257719	20020326
EP 1377593	A2	20040107	EP 2002-727484	20020326
EP 1377593	B1	20051228		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
HU 200303601	A2	20040301	HU 2003-3601	20020326
BR 2002008365	A	20040309	BR 2002-8365	20020326
JP 2004531501	T	20041014	JP 2002-576253	20020326
CN 1620461	A	20050525	CN 2002-806837	20020326
AT 314383	T	20060115	AT 2002-727484	20020326

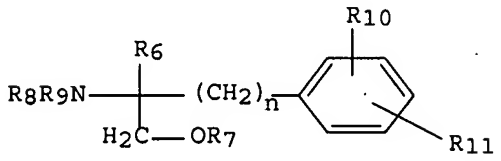
ES 2254675	T3	20060616	ES 2002-2727484		20020326
ZA 2003006914	A	20040505	ZA 2003-6914		20030904
NO 2003004291	A	20031124	NO 2003-4291		20030925
MX 2003PA08755	A	20040218	MX 2003-PA8755		20030926
IN 2003CN01514	A	20051125	IN 2003-CN1514		20030926
US 2004147490	A1	20040729	US 2004-472127		20040318
PRIORITY APPLN. INFO.:			GB 2001-7506	A	20010326
			GB 2001-7507	A	20010326
			GB 2001-8346	A	20010403
			WO 2002-EP3389	W	20020326

OTHER SOURCE(S): MARPAT 137:263181

GI



I



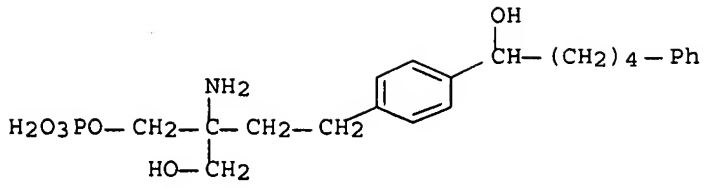
II

AB 2-Aminopropanol compds. [I; wherein m = 1, 2, 3; X = O or a direct bond; R1 = H, (C1-C6)alkyl (optionally substituted by OH, acyl, halogen, cycloalkyl, Ph or hydroxy-phenylene), (C2-C6)alkenyl, Ph (optionally substituted by OH); R2 = phosphoric acid deriv.; R3, R4, independently = H, (C1-C4)alkyl (optionally substituted by halogen or acyl); R5 = (C13-C20)alkyl, (C13-C20)alkoxy, either of which may be optionally substituted by NO2, halogen, amino, OH, etc.] and [II; wherein n = 2, 3, 4; R6 = H, (C1-C6)alkyl (optionally substituted by OH, acyl, halogen, cycloalkyl, Ph or hydroxy-phenylene), (C2-C6)alkenyl, (C2-C6)alkynyl, Ph (optionally substituted by OH); R7 = H, (C1-C4)alkyl, acyl; R8, R9, independently = H, (C1-C4)alkyl (optionally substituted by halogen or acyl); R10 = H, (C1-C4)alkyl, (C1-C4)alkoxy; R11 = (C1-C20)alkanoyl substituted by cycloalkyl, optionally substituted cycloalkyl(C1- C14)alkoxy, optionally substituted phenyl(C1-C14)alkoxy] were prepd. Thus, phosphoric acid mono-{2-amino-2-hydroxymethyl-4-[4-(5- phenylpentanoyl)phenyl]-butyl} ester was prepd. in three steps from 1-[4-(3-amino-4-hydroxy-3-hydroxymethyl-butyl)phenyl]-5-phenyl-1- pentanone. The compds. are useful in preventing or treating disorders or diseases mediated by T lymphocytes.

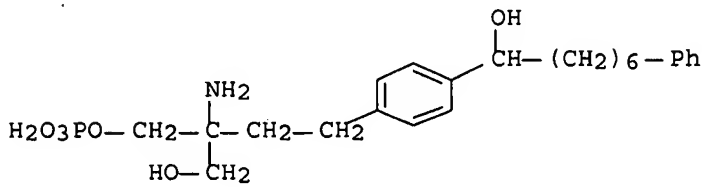
IT 463951-96-4P 463951-98-6P 463951-99-7P
463952-00-3P 463952-01-4P 463952-03-6P
463952-04-7P 463952-05-8P 463952-06-9P
463952-07-0P 463952-08-1P 463952-09-2P
463952-21-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 2-amino-propanol derivs. and use in treatment of diseases mediated by T lymphocytes)

RN 463951-96-4 CAPLUS

CN 1,3-Propanediol, 2-amino-2-[2-[4-(1-hydroxy-5-phenylpentyl)phenyl]ethyl]-, 1-(dihydrogen phosphate) (9CI) (CA INDEX NAME)

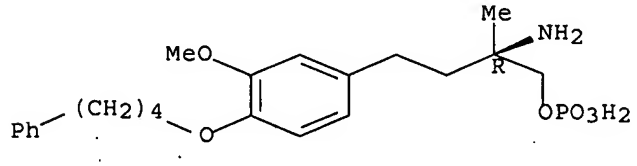


RN 463951-98-6 CAPLUS
CN 1,3-Propanediol, 2-amino-2-[2-[4-(1-hydroxy-7-phenylheptyl)phenyl]ethyl]-, 1-(dihydrogen phosphate) (9CI) (CA INDEX NAME)



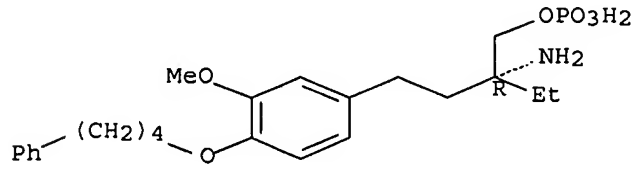
RN 463951-99-7 CAPLUS
CN Benzenebutanol, .beta.-amino-3-methoxy-.beta.-methyl-4-(4-phenylbutoxy)-, dihydrogen phosphate (ester), (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



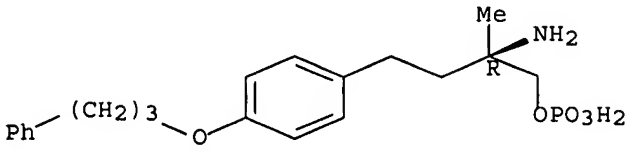
RN 463952-00-3 CAPLUS
CN Benzenebutanol, .beta.-amino-.beta.-ethyl-3-methoxy-4-(4-phenylbutoxy)-, dihydrogen phosphate (ester), (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



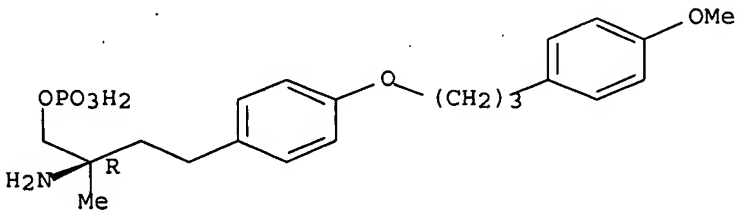
RN 463952-01-4 CAPLUS
CN Benzenebutanol, .beta.-amino-.beta.-methyl-4-(3-phenylpropoxy)-, dihydrogen phosphate (ester), (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



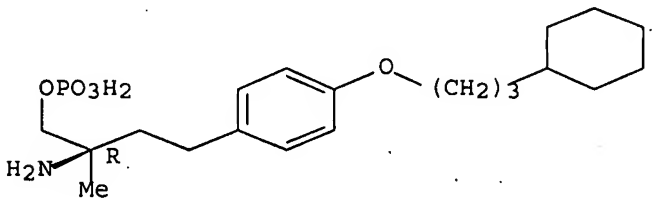
RN 463952-03-6 CAPLUS
CN Benzenebutanol, .beta.-amino-4-[3-(4-methoxyphenyl)propoxy]-.beta.-methyl-, dihydrogen phosphate (ester), (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



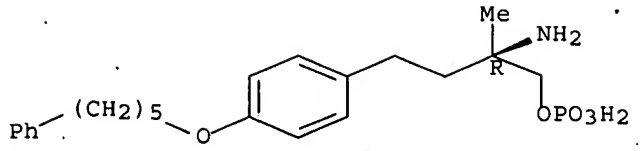
RN 463952-04-7 CAPLUS
CN Benzenebutanol, .beta.-amino-4-(3-cyclohexylpropoxy)-.beta.-methyl-, dihydrogen phosphate (ester), (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



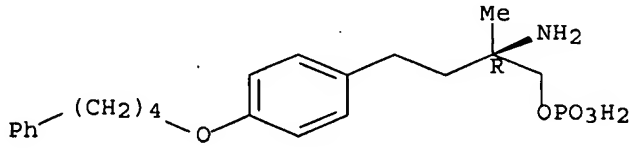
RN 463952-05-8 CAPLUS
CN Benzenebutanol, .beta.-amino-.beta.-methyl-4-[(5-phenylpentyl)oxy]-, dihydrogen phosphate (ester), (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



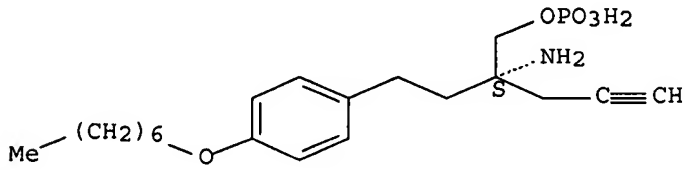
RN 463952-06-9 CAPLUS
CN Benzenebutanol, .beta.-amino-.beta.-methyl-4-(4-phenylbutoxy)-, dihydrogen phosphate (ester), (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



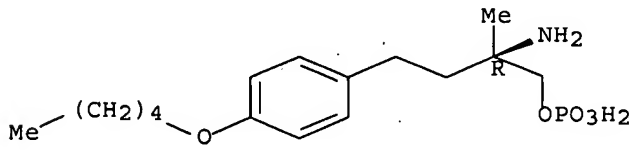
RN 463952-07-0 CAPLUS
CN Benzenebutanol, .beta.-amino-4-(heptyloxy)-.beta.-2-propynyl-, dihydrogen phosphate (ester), (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



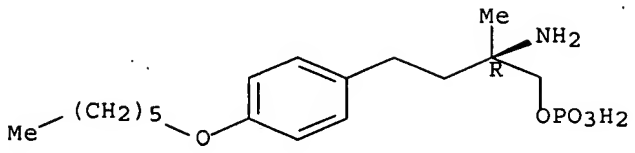
RN 463952-08-1 CAPLUS
CN Benzenebutanol, .beta.-amino-.beta.-methyl-4-(pentyloxy)-, dihydrogen phosphate (ester), (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



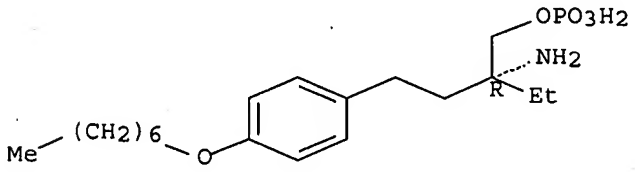
RN 463952-09-2 CAPLUS
CN Benzenebutanol, .beta.-amino-4-(hexyloxy)-.beta.-methyl-, dihydrogen phosphate (ester), (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 463952-21-8 CAPLUS
CN Benzenebutanol, .beta.-amino-.beta.-ethyl-4-(heptyloxy)-, dihydrogen phosphate (ester), (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L10 ANSWER 55 OF 58 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:708541 CAPLUS Full-text
DOCUMENT NUMBER: 138:378794
TITLE: Phytosphingosine 1-phosphate: a high affinity ligand for the S1P4/Edg-6 receptor
AUTHOR(S): Rios Candelore, Mari; Wright, Michael J.; Tota, Laurie M.; Milligan, James; Shei, Gan-ju; Bergstrom, James D.; Mandala, Suzanne M.
CORPORATE SOURCE: Merck and Company, Department of Metabolic Diseases--Diabetes, Merck Research Laboratories, Rahway, NJ, 07065, USA
SOURCE: Biochemical and Biophysical Research Communications (2002), 297(3), 600-606
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Elsevier Science
DOCUMENT TYPE: Journal
LANGUAGE: English

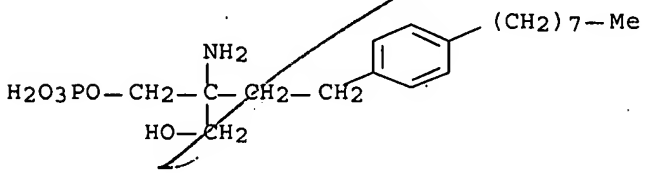
AB It has been reported recently that the phosphorylated form of the immunomodulator FTY720 activates sphingosine 1-phosphate G in-coupled receptors [1,2]. Therefore, understanding the biol. of this new class of receptors will be important in clarifying the immunol. function of bioactive lysosphingolipid ligands. The S1P4 receptor has generated interest due to its lymphoid tissue distribution. While the S1P4 receptor binds the prototypical ligand, S1P, a survey of other lysosphingolipids demonstrated that 4d-hydroxysphinganine 1-phosphate, more commonly known as phytosphingosine 1-phosphate (PhS1P), binds to S1P4 with higher affinity. Using radiolabeled S1P (S133P), the affinity of PhS1P for the S1P4 receptor is 1.6 nM, while that of S1P is nearly 50-fold lower (119.+-.20 nM). Radiolabeled PhS1P proved to be superior to S133P in routine binding assays due to improved signal-to-noise

ratio. The present study demonstrates the utility of a novel radiolabeled probe, PhS133P, for in vitro studies of the S1P4 receptor pharmacol.

IT 402615-91-2, Compound A
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(characterization of S1P4/Edg-6 receptor reveals phytosphingosine 1-phosphate is high affinity ligand)

RN 402615-91-2 CAPLUS

CN 1,3-Propanediol, 2-amino-2-[2-(4-octylphenyl)ethyl]-, 1-(dihydrogen phosphate) (CA INDEX NAME)



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 56 OF 58 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:478970 CAPLUS Full-text
DOCUMENT NUMBER: 138:49606
TITLE: The immune modulator FTY720 targets sphingosine 1-phosphate receptors
AUTHOR(S): Brinkmann, Volker; Davis, Michael D.; Heise, Christopher E.; Albert, Rainer; Cottens, Sylvain; Hof, Robert; Bruns, Christian; Prieschl, Eva; Baumruker, Thomas; Hiestand, Peter; Foster, Carolyn A.; Zollinger, Markus; Lynch, Kevin R.
CORPORATE SOURCE: Department of Transplantation, Novartis Pharma AG, Basel, CH-4002, Switz.
SOURCE: Journal of Biological Chemistry (2002), 277(24), 21453-21457
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

06/14/2002

AB Immunosuppressant drugs such as cyclosporin have allowed widespread organ transplantation, but their utility remains limited by toxicities, and they are ineffective in chronic management of autoimmune diseases such as multiple sclerosis. In contrast, the immune modulating drug FTY720 is efficacious in a variety of transplant and autoimmune models without inducing a generalized immunosuppressed state and is effective in human kidney transplantation. FTY720 elicits a lymphopenia resulting from a reversible redistribution of lymphocytes from circulation to secondary lymphoid tissues by unknown mechanisms. Using FTY720 and several analogs, we show now that FTY720 is phosphorylated by sphingosine kinase; the phosphorylated compd. is a potent agonist at four sphingosine 1-phosphate receptors and represents the therapeutic principle in a rodent model of multiple sclerosis. Our results suggest that FTY720, after phosphorylation, acts through sphingosine 1-phosphate signaling pathways to modulate chemotactic responses and lymphocyte trafficking.

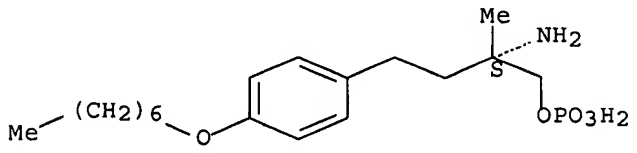
IT 479201-17-7
RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of

action); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cimmunomodulators FTY720 and analogs target sphingosine 1-phosphate receptors)

RN 479201-17-7 CAPLUS

CN Benzenebutanol, .beta.-amino-4-(heptyloxy)-.beta.-methyl-, dihydrogen phosphate (ester), (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

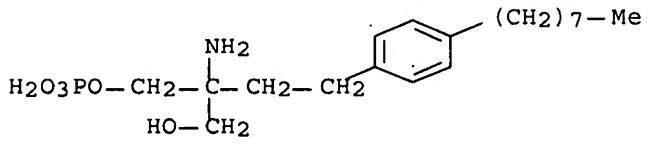


IT 402615-91-2 479201-16-6

RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(immunomodulators FTY720 and analogs target sphingosine 1-phosphate receptors)

RN 402615-91-2 CAPLUS

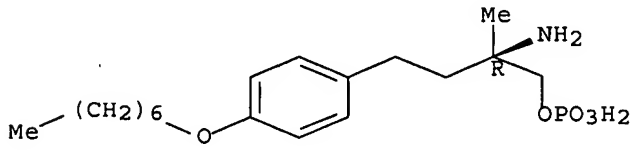
CN 1,3-Propanediol, 2-amino-2-[2-(4-octylphenyl)ethyl]-, 1-(dihydrogen phosphate) (CA INDEX NAME)



RN 479201-16-6 CAPLUS

CN Benzenebutanol, .beta.-amino-4-(heptyloxy)-.beta.-methyl-, dihydrogen phosphate (ester), (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

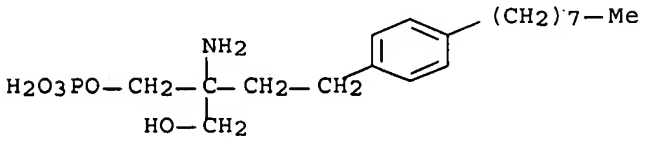


REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

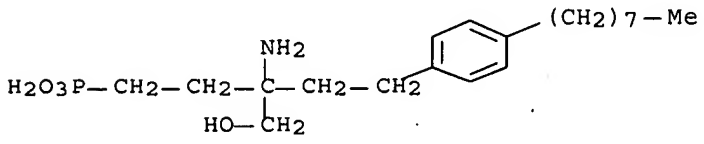
L10 ANSWER 57 OF 58 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:301209 CAPLUS Full-text

DOCUMENT NUMBER: 137:241872
TITLE: Alteration of lymphocyte trafficking by sphingosine-1-phosphate receptor agonists
AUTHOR(S): Mandala, Suzanne; Hajdu, Richard; Bergstrom, James; Quackenbush, Elizabeth; Xie, Jenny; Milligan, James; Thornton, Rosemary; Shei, Gan-Ju; Card, Deborah; Keohane, Carolann; Rosenbach, Mark; Hale, Jeffrey; Lynch, Christopher L.; Rupprecht, Kathleen; Parsons, William; Rosen, Hugh
CORPORATE SOURCE: Departments of Immunology and Rheumatology, Merck Res. Laboratories, Rahway, NJ, 07065, USA
SOURCE: Science (Washington, DC, United States) (2002), 296(5566), 346-349
CODEN: SCIEAS; ISSN: 0036-8075
PUBLISHER: American Association for the Advancement of Science
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Blood lymphocyte nos., essential for the development of efficient immune responses, are maintained by recirculation through secondary Lymphoid organs. We show that lymphocyte trafficking is altered by the lysophospholipid sphingosine-1-phosphate (S1P) and by a phosphoryl metabolite of the immunosuppressive agent FTY720. Both species were high-affinity agonists of at least four of the five S1P receptors. These agonists produce lymphopenia in blood and thoracic duct lymph by sequestration of lymphocytes in lymph nodes, but not spleen. S1P receptor agonists induced emptying of lymphoid sinuses by retention of lymphocytes on the abluminal side of sinus-lining endothelium and inhibition of egress into lymph. Inhibition of lymphocyte recirculation by activation of S1P receptors may result in therapeutically useful immunosuppression.
IT 402615-91-2 402615-93-4
RL: PAC (Pharmacological activity); BIOL (Biological study)
(alteration of lymphocyte trafficking by sphingosine-1-phosphate receptor agonists)
RN 402615-91-2 CAPLUS
CN 1,3-Propanediol, 2-amino-2-[2-(4-octylphenyl)ethyl]-, 1-(dihydrogen phosphate) (CA INDEX NAME)



RN 402615-93-4 CAPLUS
CN Phosphonic acid, [3-amino-3-(hydroxymethyl)-5-(4-octylphenyl)pentyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

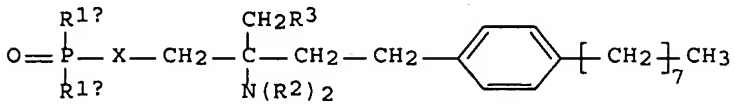
Cited ref.

L10 ANSWER 58 OF 58 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:171909 CAPLUS Full-text
DOCUMENT NUMBER: 136:216887
TITLE: Preparation of phosphate derivatives as immunosuppressants
INVENTOR(S): Mandala, Suzanne; Bergstrom, James; Hajdu, Richard; Rosen, Hugh; Parsons, William H.; Card, Deborah J.; Maccoss, Malcolm
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002018395	A1	20020307	WO 2001-US26789	20010828
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2421893	A1	20020307	CA 2001-2421893	20010828
AU 2001085331	A5	20020313	AU 2001-85331	20010828
EP 1315735	A1	20030604	EP 2001-964485	20010828
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004507552	T	20040311	JP 2002-523910	20010828
US 2002091105	A1	20020711	US 2001-942411	20010830
US 6437165	B2	20020820		

PRIORITY APPLN. INFO.: US 2000-229438P P 20000831
WO 2001-US26789 W 20010828

OTHER SOURCE(S): MARPAT 136:216887
GI



I

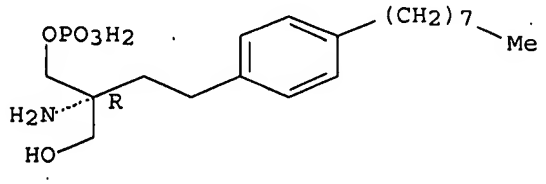
AB Immunoregulatory compds. [I; wherein: X = O, S, NR1, (CH2)1-2, optionally substituted with 1-4 halo groups (R1 = H, (C1-C4)alkyl, (C1-C4)haloalkyl); R1a

= H, OH, (C1-C4)alkyl,(C1-C4)alkyloxy, the alkyl and alkyloxy portions being optionally substituted with 1-3 halo groups; R1b = H, OH, (C1-C4)alkyl, (C1-C4)haloalkyl; R2 = H, (C1-C4)alkyl, (C1-C4)haloalkyl; and R3 = H, OH, halo, (C1-C4)alkyloxy, (C1-C4)haloalkyloxy], as well as the pharmaceutically acceptable salts and hydrates thereof, are disclosed. Thus, a multistep prepn. of 3-amino-3-hydroxymethyl-5-(4- octylphenyl)pentylphosphonic acid is described. The compds. are useful as immunosuppressants, particularly in the treatment of bone marrow and organ transplant rejection. Pharmaceutical compns. and methods of use are included.

IT 402616-23-3P 402616-26-6P
RL: PAC (Pharmacological activity); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of phosphate derivs. as immunosuppressants)

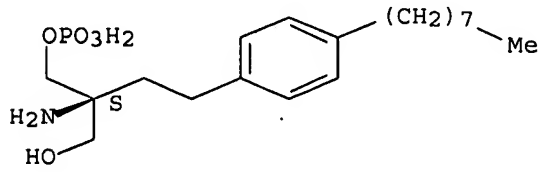
RN 402616-23-3 CAPLUS
CN 1,3-Propanediol, 2-amino-2-[2-(4-octylphenyl)ethyl]-, mono(dihydrogen phosphate) (ester), (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



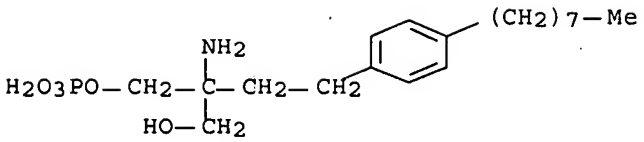
RN 402616-26-6 CAPLUS
CN 1,3-Propanediol, 2-amino-2-[2-(4-octylphenyl)ethyl]-, mono(dihydrogen phosphate) (ester), (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

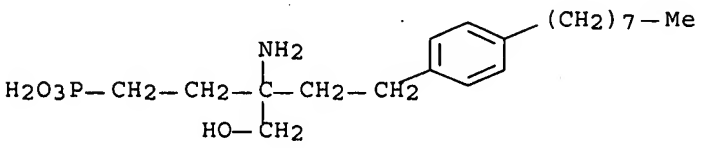


IT 402615-91-2P 402615-93-4P 402616-08-4P
402616-10-8P 402616-25-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of phosphate derivs. as immunosuppressants)

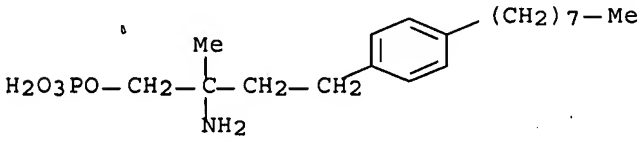
RN 402615-91-2 CAPLUS
CN 1,3-Propanediol, 2-amino-2-[2-(4-octylphenyl)ethyl]-, 1-(dihydrogen phosphate) (CA INDEX NAME)



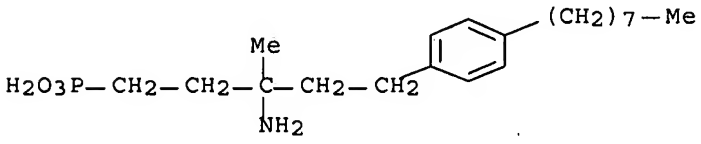
RN 402615-93-4 CAPLUS
CN Phosphonic acid, [3-amino-3-(hydroxymethyl)-5-(4-octylphenyl)pentyl]- (9CI) (CA INDEX NAME)



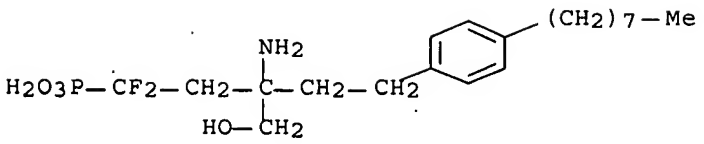
RN 402616-08-4 CAPLUS
CN Benzenebutanol, .beta.-amino-.beta.-methyl-4-octyl-, dihydrogen phosphate (ester) (9CI) (CA INDEX NAME)



RN 402616-10-8 CAPLUS
CN Phosphonic acid, [3-amino-3-methyl-5-(4-octylphenyl)pentyl]- (9CI) (CA INDEX NAME)



RN 402616-25-5 CAPLUS
CN Phosphonic acid, [3-amino-1,1-difluoro-3-(hydroxymethyl)-5-(4-octylphenyl)pentyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s l10 and immune
218512 IMMUNE
6 IMMUNES
218514 IMMUNE
(IMMUNE OR IMMUNES)
L11 9 L10 AND IMMUNE

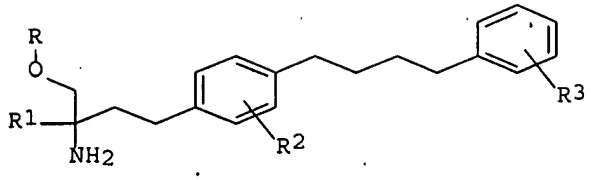
=> d ibib abs hitstr tot

L11 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1279843 CAPLUS Full-text
DOCUMENT NUMBER: 146:45290
TITLE: Preparation of 4-[4-(4-phenylbutyl)phenyl]-2-aminobutanol derivatives as immunosuppressants
INVENTOR(S): Kiuchi, Masatoshi; Kobayashi, Nobutaka; Sugahara, Kunio; Nakamura, Mitsuharu
PATENT ASSIGNEE(S): Mitsubishi Pharma Corporation, Japan
SOURCE: PCT Int. Appl., 108pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006129688	A1	20061207	WO 2006-JP310841	20060531

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: JP 2005-159672 A 20050531
OTHER SOURCE(S): MARPAT 146:45290
GI

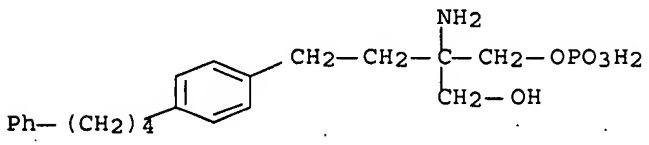


I

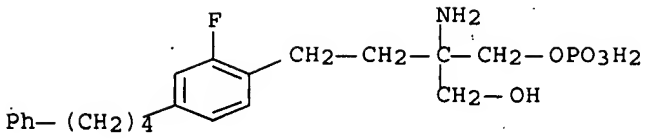
AB The title compds. [I; R = H, P(O)(OH)2; R1 = optionally hydroxylated or halogenated C1-4 alkyl; R2, R3 = H, halo, optionally halogenated C1-4 alkyl; R3 = hydrogen atom or halogen atom or an optionally halogenated C1-4 alkyl] or pharmaceutically acceptable acid adduct salts, hydrates, or solvates thereof are prepd. There compds. excel in immunosuppressive action, anti-rejection activity, etc. and are relieved in bradycardia and other side effects. These compds. are useful for the prevention or suppression of acute and/or chronic rejection occurring in transplantation of organs, liver, heart, kidney, or bone marrow or the treatment and/or prevention of guest-vs.-host disease in bone marrow transplantation, chronic articular rheumatism, systemic erythematosus, multiple sclerosis, type I or type II diabetes, etc. Thus, coupling of 1-acetamido-1,3- bisacetoxy-2-[2-(4-bromophenyl)ethyl]propane with 4-phenyl-1-butyne in the presence of 2-(dicyclohexylphosphino)-2',4',6'-triisopropyl-1,1'-biphenyl and dichlorobis(acetonitrile)palladium(II) and Cs2CO3 in MeCN under refluxing for 6.5 h gave acetic acid 2-acetoxymethyl-2-acetylamino-4-[4-(4- phenylbut-1-ynyl)phenyl]butyl ester which underwent hydrogenation over 10% Pd-C in MeOH at room temp. for 7 h to give acetic acid 2-acetoxymethyl-2-acetylamino-4-[4-(4-phenylbutyl)phenyl]butyl ester(II). Hydrolysis of II with a mixt. of 4 M aq. NaOH soln., MeOH, and THF under refluxing for 6.5 h followed by treatment with 4 M HCl/EtOAc gave 2-amino-2-[2-[4-(4-phenylbutyl)phenyl]ethyl]propane-1,3-diol hydrochloride (III). III in vivo showed IC50 of 0.02 mg/kg body wt. against decreasing lymphocyte count in peripheral blood in mice.

IT 916517-24-3P 916517-68-5P 916517-71-0P
916517-74-3P 916517-77-6P 916517-80-1P
916517-82-3P 916517-84-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 4-[4-(4-phenylbutyl)phenyl]-2-aminobutanol derivs. as immunosuppressants)

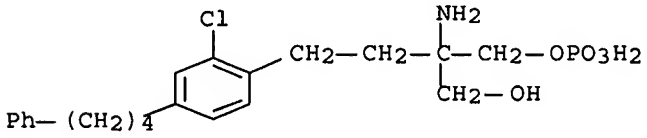
RN 916517-24-3 CAPLUS
CN 1,3-Propanediol, 2-amino-2-[2-[4-(4-phenylbutyl)phenyl]ethyl]-, 1-(dihydrogen phosphate) (CA INDEX NAME)



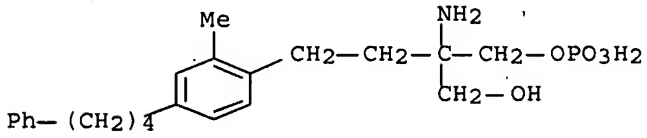
RN 916517-68-5 CAPLUS
CN 1,3-Propanediol, 2-amino-2-[2-[2-fluoro-4-(4-phenylbutyl)phenyl]ethyl]-, 1-(dihydrogen phosphate) (CA INDEX NAME)



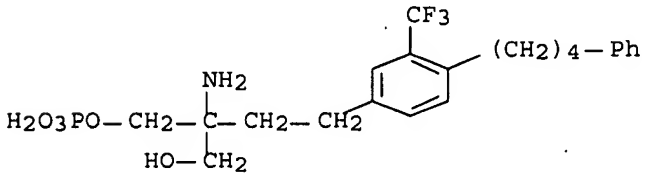
RN 916517-71-0 CAPLUS
CN 1,3-Propanediol, 2-amino-2-[2-[2-chloro-4-(4-phenylbutyl)phenyl]ethyl]-, 1-(dihydrogen phosphate) (CA INDEX NAME)



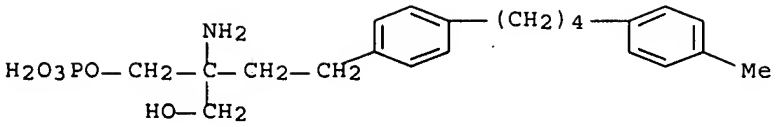
RN 916517-74-3 CAPLUS
CN 1,3-Propanediol, 2-amino-2-[2-[2-methyl-4-(4-phenylbutyl)phenyl]ethyl]-, 1-(dihydrogen phosphate) (CA INDEX NAME)



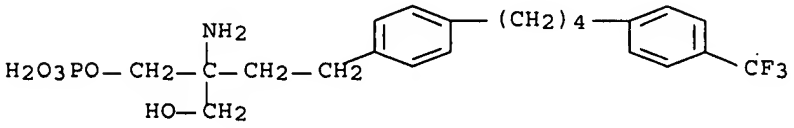
RN 916517-77-6 CAPLUS
CN 1,3-Propanediol, 2-amino-2-[2-[4-(4-phenylbutyl)-3-(trifluoromethyl)phenyl]ethyl]-, 1-(dihydrogen phosphate) (CA INDEX NAME)



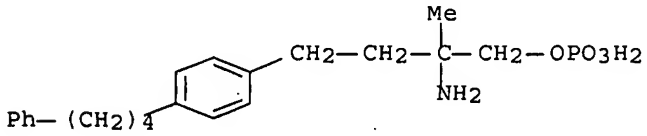
RN 916517-80-1 CAPLUS
CN 1,3-Propanediol, 2-amino-2-[2-[4-[4-(4-methylphenyl)butyl]phenyl]ethyl]-, 1-(dihydrogen phosphate) (CA INDEX NAME)



RN 916517-82-3 CAPLUS
CN 1,3-Propanediol, 2-amino-2-[2-[4-[4-[4-(trifluoromethyl)phenyl]butyl]phenyl]ethyl]-, 1-(dihydrogen phosphate) (CA INDEX NAME)



RN 916517-84-5 CAPLUS
CN Benzenebutanol, .beta.-amino-.beta.-methyl-4-(4-phenylbutyl)-, 1-(dihydrogen phosphate) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1107194 CAPLUS Full-text
DOCUMENT NUMBER: 146:77243
TITLE: Comparative quantification of sphingolipids and analogs in biological samples by high-performance liquid chromatography after chloroform extraction
AUTHOR(S): Andreani, Paul; Graeler, Markus H.
CORPORATE SOURCE: Institute for Immunology, Hannover Medical School, Hanover, 30625, Germany
SOURCE: Analytical Biochemistry (2006), 358(2), 239-246
CODEN: ANBCA2; ISSN: 0003-2697
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

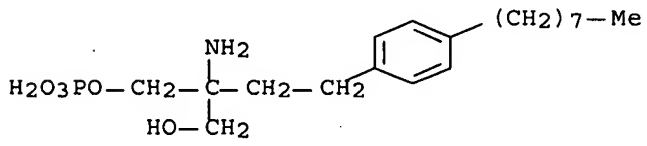
AB Sphingosine 1-phosphate (S1P) is an extra- and intracellular messenger that specifically activates five G-protein-coupled cell surface receptors designated S1P1-5. The S1P1 receptor is particularly important for the maintenance of immune surveillance by regulating egress of lymphocytes from thymus and secondary lymphoid organs. S1P is generated through phosphorylation of sphingosine which is catalyzed by sphingosine kinase types

1 and 2. The immunosuppressant and sphingosine analog Fingolimod (2-amino-2-(2-[4-octylphenyl]ethyl)-1,3-propanediol, FTY720) can also be phosphorylated and induces lymphopenia by downregulating cell surface expression of the S1P1 receptor on lymphocytes. To analyze the role of S1P in lymphocyte circulation and distribution we established a high-performance-liq.-chromatog.-based method for parallel detection and quantification of Fingolimod, sphingosine, and dihydrosphingosine together with their phosphorylated derivs. Fingolimod-phosphate, S1P, and dihydrosphingosine 1-phosphate. Phosphorylated and nonphosphorylated lipids were efficiently isolated from biol. samples such as cells, tissues, serum, plasma, and media by simple chloroform extn. Fluorescence labeling with 9-fluorenylmethyl chloroformiate ensured high selectivity and enhanced sensitivity for sphingolipid detection. The described method provides an accurate approach to investigate phosphorylation, dephosphorylation, hydrolyzation, and dehydrolyzation of sphingolipids and analogs. In addn. it works independently from enzymic conversions, measuring actual concns. rather than enzymic activities.

IT 402615-91-2, FTY 720 phosphate
RL: ANT (Analyte); BSU (Biological study, unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological study)
(FTY-P; comparative quantification of sphingolipids and analogs in biol. samples by high-performance liq. chromatog. after chloroform extn.)

RN 402615-91-2 CAPLUS

CN 1,3-Propanediol, 2-amino-2-[2-(4-octylphenyl)ethyl]-, 1-(dihydrogen phosphate) (CA INDEX NAME)



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:1061349 CAPLUS Full-text

DOCUMENT NUMBER: 143:415807

TITLE: The Immune Modulator FTY720 Inhibits Sphingosine-1-phosphate Lyase Activity

AUTHOR(S): Bandhuvula, Padmavathi; Tam, Yuen Yee; Oskouian, Babak; Saba, Julie D.

CORPORATE SOURCE: Oakland Research Institute, Children's Hospital, Oakland, CA, 94609-1673, USA

SOURCE: Journal of Biological Chemistry (2005), 280(40), 33697-33700
CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

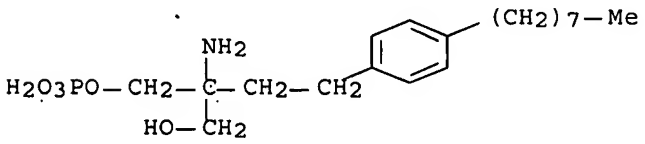
AB FTY720 is a novel immunomodulatory agent that inhibits lymphocyte trafficking and prevents allograft rejection. FTY720 is phosphorylated in vivo, and the phosphorylated drug acts as agonist for a family of G protein-coupled receptors that recognize sphingosine 1-phosphate. Evidence suggests that FTY720-phosphate-induced activation of S1P1 is responsible for its mechanism

of action. FTY720 was rationally designed by modification of myriocin, a naturally occurring sphingoid base analog that causes immunosuppression by interrupting sphingolipid metab. In this study, we examd. interactions between FTY720, FTY720-phosphate, and sphingosine-1-phosphate lyase, the enzyme responsible for irreversible sphingosine 1-phosphate degrdn. FTY720-phosphate was stable in the presence of active sphingosine-1-phosphate lyase, demonstrating that the lyase does not contribute to FTY720 catabolism. Conversely, FTY720 inhibited sphingosine-1-phosphate lyase activity in vitro. Treatment of mice with FTY720 inhibited tissue sphingosine-1-phosphate lyase activity within 12 h, whereas lyase gene and protein expression were not significantly affected. Tissue sphingosine 1-phosphate levels remained stable or increased throughout treatment. These studies raise the possibility that disruption of sphingosine 1-phosphate metab. may account for some effects of FTY720 on immune function and that sphingosine-1-phosphate lyase may be a potential target for immunomodulatory therapy.

IT 402615-91-2, FTY 720P
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(immune modulator FTY720 inhibits sphingosine-1-phosphate lyase activity)

RN 402615-91-2 CAPLUS

CN 1,3-Propanediol, 2-amino-2-[2-(4-octylphenyl)ethyl]-, 1-(dihydrogen phosphate) (CA INDEX NAME)



REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:403930 CAPLUS Full-text

DOCUMENT NUMBER: 141:99305

TITLE: Potent S1P receptor agonists replicate the pharmacologic actions of the novel immune modulator FTY720

AUTHOR(S): Hale, Jeffrey J.; Neway, William; Mills, Sander G.; Hajdu, Richard; Keohane, Carol Ann; Rosenbach, Mark; Milligan, James; Shei, Gan-Ju; Chrebet, Gary; Bergstrom, James; Card, Deborah; Koo, Gloria C.; Koprak, Sam L.; Jackson, Jesse J.; Rosen, Hugh; Mandala, Suzanne

CORPORATE SOURCE: Department of Medicinal Chemistry, Merck Research Laboratories, Rahway, NJ, 07065, USA

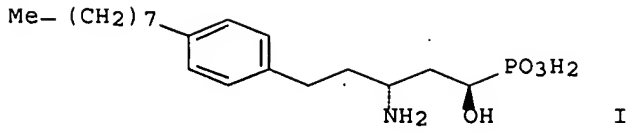
SOURCE: Bioorganic & Medicinal Chemistry Letters (2004), 14(12), 3351-3355
CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



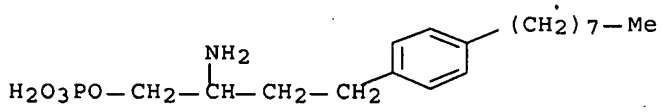
I

AB Alteration in lymphocyte trafficking and prevention of graft rejection in rodents obsd. on exposure to FTY720 or its corresponding phosphate ester can be induced by the systemic administration of potent sphingosine-1-phosphate receptor agonists exemplified by I. The similar S1P receptor profiles of the FTY720 phosphate ester and I coupled with their comparable potency in vivo supports a connection between S1P receptor agonism and immunosuppressive efficacy.

IT 596819-80-6P 597340-18-6P 597340-22-2P
597340-27-7P 597340-33-5P
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(potent sphingosine-1-phosphate receptor agonists replicate the pharmacol. actions of novel immunosuppressant FTY720 in prevention of graft rejection in relation to alteration in lymphocyte trafficking and pharmacokinetics)

RN 596819-80-6 CAPLUS

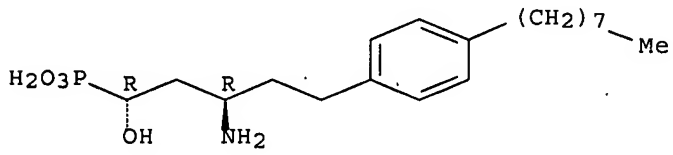
CN Benzenebutanol, .beta.-amino-4-octyl-, dihydrogen phosphate (ester) (9CI) (CA INDEX NAME)



RN 597340-18-6 CAPLUS

CN Phosphonic acid, [(1R,3R)-3-amino-1-hydroxy-5-(4-octylphenyl)pentyl]- (9CI) (CA INDEX NAME)

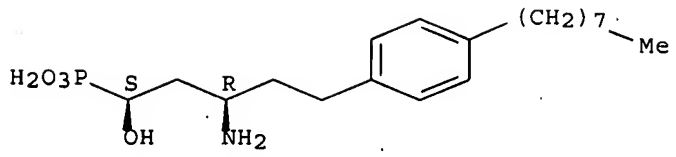
Absolute stereochemistry.



RN 597340-22-2 CAPLUS

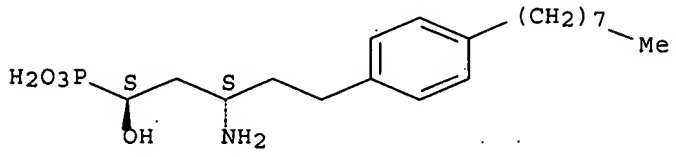
CN Phosphonic acid, [(1S,3R)-3-amino-1-hydroxy-5-(4-octylphenyl)pentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



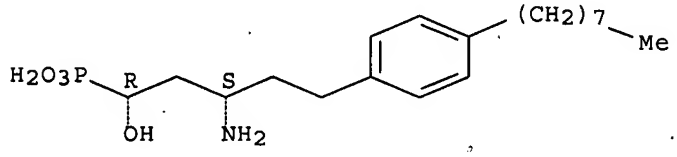
RN 597340-27-7 CAPLUS
CN Phosphonic acid, [(1S,3S)-3-amino-1-hydroxy-5-(4-octylphenyl)pentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



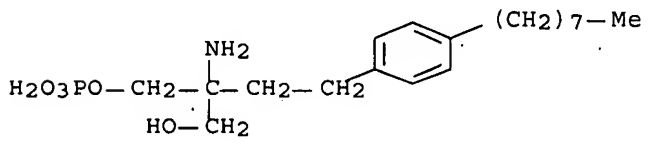
RN 597340-33-5 CAPLUS
CN Phosphonic acid, [(1R,3S)-3-amino-1-hydroxy-5-(4-octylphenyl)pentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



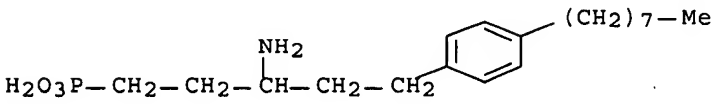
IT 402615-91-2
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(potent sphingosine-1-phosphate receptor agonists replicate the pharmacol. actions of novel immunosuppressant FTY720 in prevention of graft rejection in relation to alteration in lymphocyte trafficking and pharmacokinetics)

RN 402615-91-2 CAPLUS
CN 1,3-Propanediol, 2-amino-2-[2-(4-octylphenyl)ethyl]-, 1-(dihydrogen phosphate) (CA INDEX NAME)

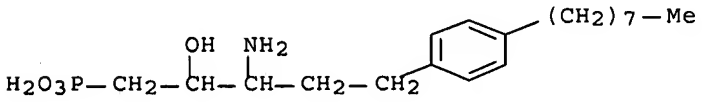


IT 596819-84-0P 596819-85-1P 596819-90-8P
596819-92-0P 717888-67-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(potent sphingosine-1-phosphate receptor agonists replicate the pharmacol. actions of novel immunosuppressant FTY720 in prevention of graft rejection in relation to alteration in lymphocyte trafficking and pharmacokinetics)

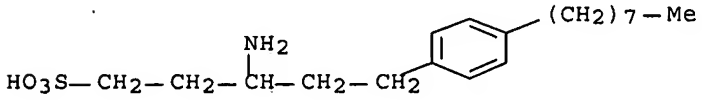
RN 596819-84-0 CAPLUS
CN Phosphonic acid, [3-amino-5-(4-octylphenyl)pentyl]- (9CI) (CA INDEX NAME)



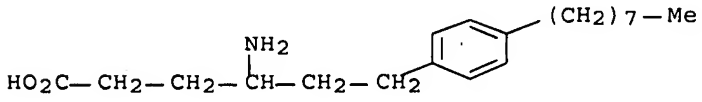
RN 596819-85-1 CAPLUS
CN Pentitol, 3-amino-1,2,3,5-tetradeoxy-1-(4-octylphenyl)-5-phosphono- (9CI) (CA INDEX NAME)



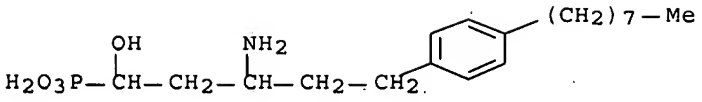
RN 596819-90-8 CAPLUS
CN Benzenepentanesulfonic acid, .gamma.-amino-4-octyl- (9CI) (CA INDEX NAME)



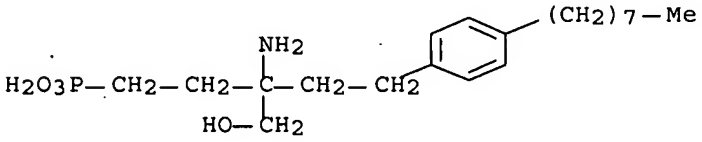
RN 596819-92-0 CAPLUS
CN Benzenehexanoic acid, .gamma.-amino-4-octyl- (9CI) (CA INDEX NAME)



RN 717888-67-0 CAPLUS
CN Phosphonic acid, [3-amino-1-hydroxy-5-(4-octylphenyl)pentyl]- (9CI) (CA INDEX NAME)



IT 402615-93-4
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(potent sphingosine-1-phosphate receptor agonists replicate the pharmacol. actions of novel immunosuppressant FTY720 in prevention of graft rejection in relation to alteration in lymphocyte trafficking and pharmacokinetics)
RN 402615-93-4 CAPLUS
CN Phosphonic acid, [3-amino-3-(hydroxymethyl)-5-(4-octylphenyl)pentyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

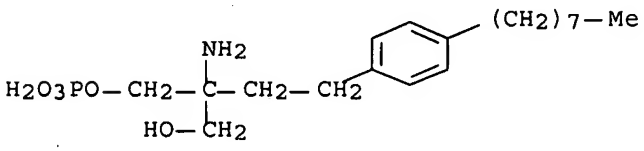
L11 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:368306 CAPLUS Full-text
DOCUMENT NUMBER: 141:99302
TITLE: Immune cell regulation and cardiovascular effects of sphingosine 1-phosphate receptor agonists in rodents are mediated via distinct receptor subtypes
AUTHOR(S): Forrest, M.; Sun, S.-Y.; Hajdu, R.; Bergstrom, J.; Card, D.; Doherty, G.; Hale, J.; Keohane, C.; Meyers, C.; Milligan, J.; Mills, S.; Nomura, N.; Rosen, H.; Rosenbach, M.; Shei, G.-J.; Singer, I. I.; Tian, M.; West, S.; White, V.; Xie, J.; Proia, R. L.; Mandala, S.
CORPORATE SOURCE: Departments of Immunology and Rheumatology, Pharmacology, and Medicinal Chemistry, Merck Research Laboratories, Rahway, NJ, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2004), 309(2), 758-768
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Sphingosine 1-phosphate (S1P) is a bioactive lysolipid with pleiotropic functions mediated through a family of G protein-coupled receptors, S1P1,2,3,4,5. Physiol. effects of S1P receptor agonists include regulation of cardiovascular function and immunosuppression via redistribution of

lymphocytes from blood to secondary lymphoid organs. The phosphorylated metabolite of the immunosuppressant agent FTY720 (2-amino-2-(2-[4-octylphenyl]ethyl)-1,3-propanediol) and other phosphonate analogs with differential receptor selectivity were investigated. No significant species differences in compd. potency or rank order of activity on receptors cloned from human, murine, and rat sources were obsd. All synthetic analogs were high-affinity agonists on S1P1, with IC50 values for ligand binding between 0.3 and 14 nM. The correlation between S1P1 receptor activation and the ED50 for lymphocyte redn. was highly significant ($p < 0.001$) and lower for the other receptors. In contrast to S1P1-mediated effects on lymphocyte recirculation, three lines of evidence link S1P3 receptor activity with acute toxicity and cardiovascular regulation: compd. potency on S1P3 correlated with toxicity and bradycardia; the shift in potency of phosphorylated-FTY720 for inducing lymphopenia vs. bradycardia and hypertension was consistent with affinity for S1P1 relative to S1P3; and toxicity, bradycardia, and hypertension were absent in S1P3-/- mice. Blood pressure effects of agonists in anesthetized rats were complex, whereas hypertension was the predominant effect in conscious rats and mice. Immunolocalization of S1P3 in rodent heart revealed abundant expression on myocytes and perivascular smooth muscle cells consistent with regulation of bradycardia and hypertension, whereas S1P1 expression was restricted to the vascular endothelium.

IT 402615-91-2
RL: PAC (Pharmacological activity); BIOL (Biological study)
(immune cell regulation and cardiovascular effects of sphingosine 1-phosphate receptor agonists in rodents are mediated via distinct receptor subtypes)

RN 402615-91-2 CAPLUS

CN 1,3-Propanediol, 2-amino-2-[2-(4-octylphenyl)ethyl]-, 1-(dihydrogen phosphate) (CA INDEX NAME)



REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:719274 CAPLUS Full-text

DOCUMENT NUMBER: 139:246116

TITLE: Preparation of aminoalkylphosphonates and related compounds as EDG receptor agonists

INVENTOR(S): Doherty, George A.; Hale, Jeffrey J.

PATENT ASSIGNEE(S): Merck & Co., Inc., USA

SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003074008	A2	20030912	WO 2003-US7262	20030225

WO 2003074008 A3 · 20040226
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

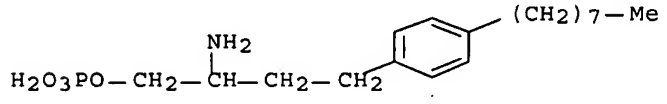
CA 2477449	A1	20030912	CA 2003-2477449		20030225
AU 2003218056	A1	20030916	AU 2003-218056		20030225
EP 1482896	A2	20041208	EP 2003-714037		20030225
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
US 2005107345	A1	20050519	US 2003-505268		20030225
JP 2005531508	T	20051020	JP 2003-572530		20030225
PRIORITY APPLN. INFO.:			US 2002-360605P	P	20020301
			WO 2003-US7262	W	20030225

OTHER SOURCE(S): MARPAT 139:246116

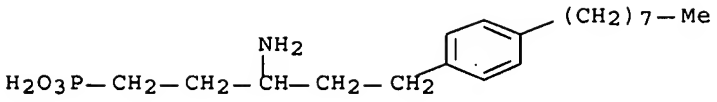
AB The present invention encompasses title compds., A-X[CR1R2]mCHNH2[CR3R4]pC(R9)3 (m = 1-4; p = 9-20; X = bond, O, NH, S(O)k, k = 0-2; A = CO2H, PO3H2, PO2H2, SO3H, five membered nitrogen contg. heterocyclyl, etc.; two R1 or R3 groups on adjacent carbon may be joined together to form a double bond; R2, R3, R4 = H, halo, OH, CO2H, C1-4 alkyl, alkoxy, alkylthio, aryl, etc.; R1-R4 = residing on the same carbon optionally joined together to form a carbonyl group, etc.; R9 = H, halo, OH, C1-4 alkoxy, alkylthio, C3-7 cycloalkyl, etc.); as well as the pharmaceutically acceptable salts and hydrates thereof. The compds. are useful for treating immune mediated diseases and conditions, such as bone marrow, organ and tissue transplant rejection. Pharmaceutical compns. and methods of use are included. Thus, prepn. of (+/-)-2-amino-4-(4-(octylphenyl))butanol, O-phosphate was described in five steps starting from di-Et 2-acetamido-2-(2-(4-octylphenyl)ethyl)propanedioate.

IT 596819-80-6P 596819-84-0P 596819-85-1P
596819-88-4P 596819-89-5P 596819-90-8P
596819-92-0P 596819-94-2P 596819-95-3P
596819-96-4P 596819-97-5P 596819-99-7P
596820-00-7P 596820-06-3P 596820-07-4P
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of aminoalkylphosphonates and related compds. as EDG receptor agonists)

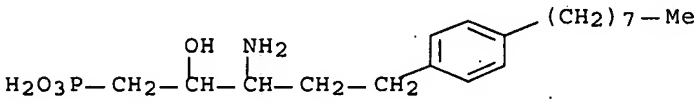
RN 596819-80-6 CAPLUS
CN Benzenebutanol, .beta.-amino-4-octyl-, dihydrogen phosphate (ester) (9CI) (CA INDEX NAME)



RN 596819-84-0 CAPLUS
CN Phosphonic acid, [3-amino-5-(4-octylphenyl)pentyl]- (9CI) (CA INDEX NAME)



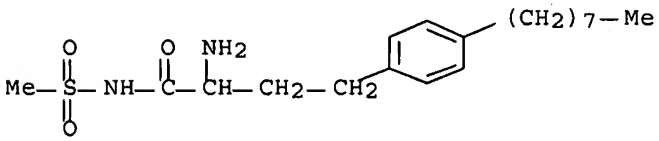
RN 596819-85-1 CAPLUS
CN Pentitol, 3-amino-1,2,3,5-tetradeoxy-1-(4-octylphenyl)-5-phosphono- (9CI) (CA INDEX NAME)



RN 596819-88-4 CAPLUS
CN Benzenebutanamide, .alpha.-amino-N-(methylsulfonyl)-4-octyl-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

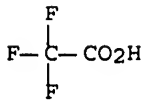
CM 1

CRN 596819-87-3
CMF C19 H32 N2 O3 S

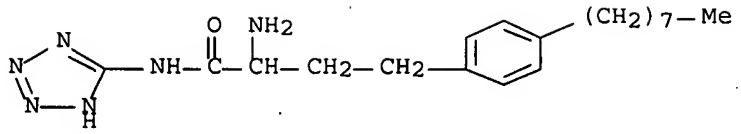


CM 2

CRN 76-05-1
CMF C2 H F3 O2

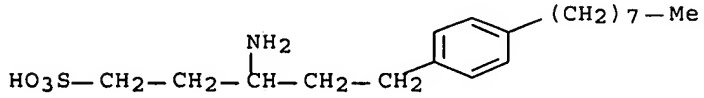


RN 596819-89-5 CAPLUS
CN Benzenebutanamide, .alpha.-amino-4-octyl-N-1H-tetrazol-5-yl-, monohydrochloride (9CI) (CA INDEX NAME)

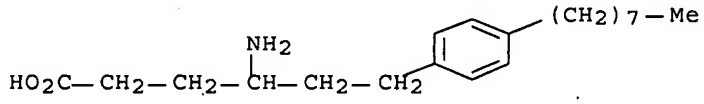


● HCl

RN 596819-90-8 CAPLUS
CN Benzenepentanesulfonic acid, .gamma.-amino-4-octyl- (9CI). (CA INDEX NAME)



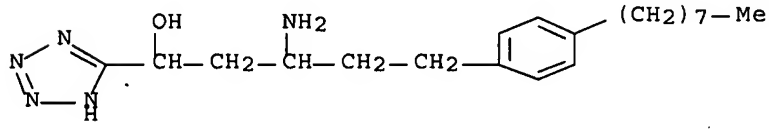
RN 596819-92-0 CAPLUS
CN Benzenehexanoic acid, .gamma.-amino-4-octyl- (9CI) (CA INDEX NAME)



RN 596819-94-2 CAPLUS
CN 1H-Tetrazole-5-methanol, .alpha.-[2-amino-4-(4-octylphenyl)butyl]-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

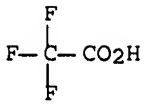
CM 1

CRN 596819-93-1
CMF C20 H33 N5 O



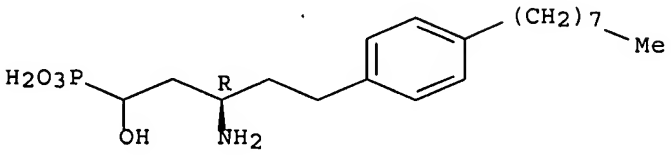
CM 2

CRN 76-05-1
CMF C2 H F3 O2



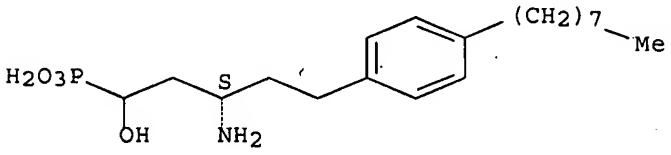
RN 596819-95-3 CAPLUS
CN Phosphonic acid, [(3R)-3-amino-1-hydroxy-5-(4-octylphenyl)pentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



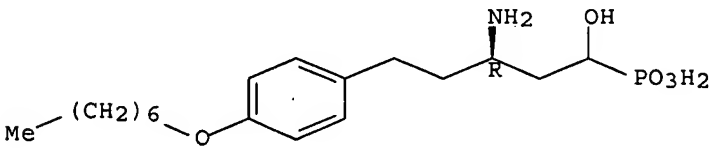
RN 596819-96-4 CAPLUS
CN Phosphonic acid, [(3S)-3-amino-1-hydroxy-5-(4-octylphenyl)pentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



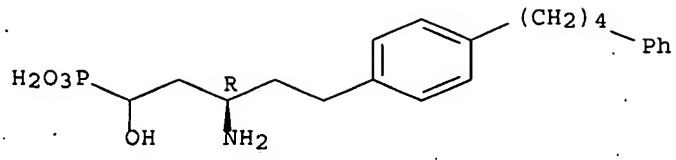
RN 596819-97-5 CAPLUS
CN Phosphonic acid, [(3R)-3-amino-5-[4-(heptyloxy)phenyl]-1-hydroxypentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



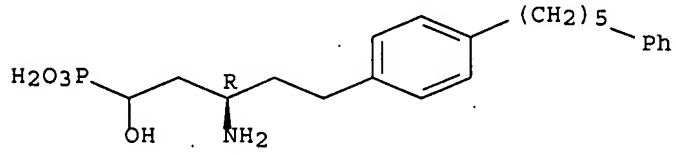
RN 596819-99-7 CAPLUS
CN Phosphonic acid, [(3R)-3-amino-1-hydroxy-5-[4-(4-phenylbutyl)phenyl]pentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



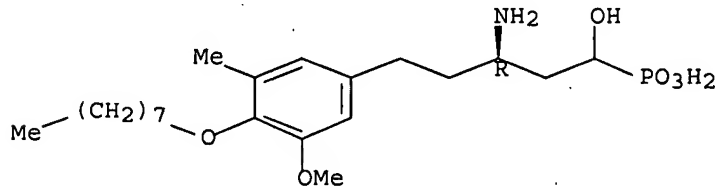
RN 596820-00-7 CAPLUS
CN Phosphonic acid, [(3R)-3-amino-1-hydroxy-5-[4-(5-phenylpentyl)phenyl]pentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



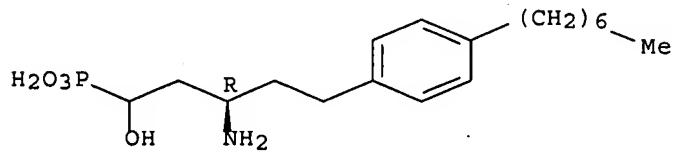
RN 596820-06-3 CAPLUS
CN Phosphonic acid, [(3R)-3-amino-1-hydroxy-5-[3-methoxy-5-methyl-4-(octyloxy)phenyl]pentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 596820-07-4 CAPLUS
CN Phosphonic acid, [(3R)-3-amino-5-(4-heptylphenyl)-1-hydroxypentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:719253 CAPLUS Full-text

Current

DOCUMENT NUMBER: 139:245479
TITLE: Preparation of aminoalkylphosphonates and related compounds as EDG receptor agonists
INVENTOR(S): Budhu, Richard J.; Doherty, George A.; Hale, Jeffrey J.; Lynch, Christopher L.; Mills, Sander G.; Neway, William E., III
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 90 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003073986	A2	20030912	WO 2003-US5947		20030227
WO 2003073986	A3	20040527			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2477423	A1	20030912	CA 2003-2477423		20030227
AU 2003217764	A1	20030916	AU 2003-217764		20030227
EP 1482895	A2	20041208	EP 2003-713727		20030227
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
JP 2005531506	T	20051020	JP 2003-572508		20030227
US 2006089334	A1	20060427	US 2004-505257		20040819
PRIORITY APPLN. INFO.:			US 2002-360663P	P	20020301
			WO 2003-US5947	W	20030227

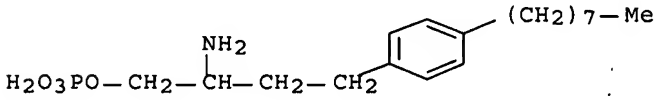
OTHER SOURCE(S): MARPAT 139:245479

AB AX(CR1R2)mCH(NH2)(CR3R4)nArBC [A = CO2H, P(O)(OH)2, PH(O)(OH), SO3H, P(O)R5OH, 5-membered N heterocycle; X = bond, O, NH, S, S, S(O), SO2; R1-R4 = H, halogen, OH, CO2H, (un)substituted alkyl, alkoxy, alkylthio, aryl; R1R2, R3R4 = O; m = 1-4; n = 0-4; R5 = (un)substituted alkyl, aryl; Ar = Ph, naphthyl; C = (un)substituted alkyl, alkoxy, acyl, hydroxyalkyl, Ph, heterocyclic, bond; when C = bond, B = (un)substituted Ph, alkyl, alkenyl, alkynyl, OH, SH, acyl, CONH2, NH2; when C = Ph, heterocyclic, B = (un)substituted alkyl, alkoxy, acyl, CO, CH(OH), C6H4, heterocyclic; when C = alkyl, alkoxy, acyl, B = (un)substituted C6H4, heterocyclic] were prepd. for use as EDG receptor antagonists useful for treating immune mediated diseases and conditions, such as bone marrow, organ and tissue transplant rejection (no data). Thus, 4-Me(CH2)7C6H4CH2CH2C(NHAc)(CO2Et)2 was hydrolyzed and decarboxylated to 4-Me(CH2)7C6H4CH2CH2CH(NH2)CO2H which was N-benzyloxycarbonylated, reduced to 4-Me(CH2)7C6H4CH2CH2CH(NHCbz)CH2OH, phosphorylated (MeCH)2NP(OCH2Ph)2, and deblocked to give 4-Me(CH2)7C6H4CH2CH2CH(NH2)CH2OP(O)(OH)2.

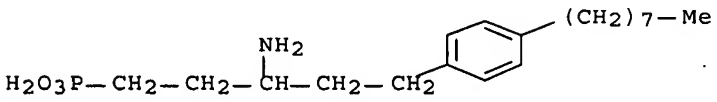
IT 596819-80-6P 596819-84-0P 596819-85-1P
596819-88-4P 596819-89-5P 596819-90-8P
596819-92-0P 596819-97-5P 596819-99-7P
596820-00-7P 596820-06-3P 596820-07-4P
597340-06-2P 597340-13-1P 597340-18-6P
597340-22-2P 597340-27-7P 597340-33-5P
597342-93-3P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of aminoalkylphosphonates and related compds. as EDG receptor agonists)

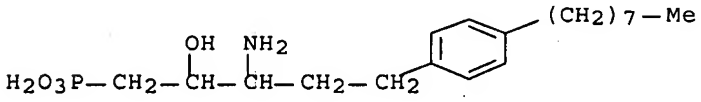
RN 596819-80-6 CAPLUS
CN Benzenebutanol, .beta.-amino-4-octyl-, dihydrogen phosphate (ester) (9CI) (CA INDEX NAME)



RN 596819-84-0 CAPLUS
CN Phosphonic acid, [3-amino-5-(4-octylphenyl)pentyl]- (9CI) (CA INDEX NAME)



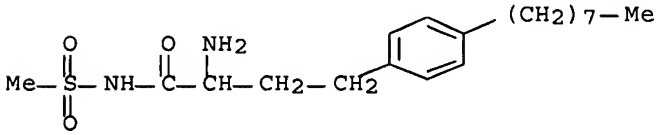
RN 596819-85-1 CAPLUS
CN Pentitol, 3-amino-1,2,3,5-tetradeoxy-1-(4-octylphenyl)-5-phosphono- (9CI) (CA INDEX NAME)



RN 596819-88-4 CAPLUS
CN Benzenebutanamide, .alpha.-amino-N-(methylsulfonyl)-4-octyl-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

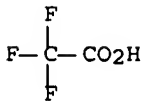
CM 1

CRN 596819-87-3
CMF C19 H32 N2 O3 S

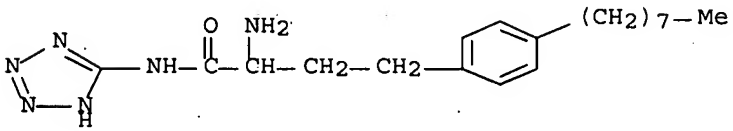


CM 2

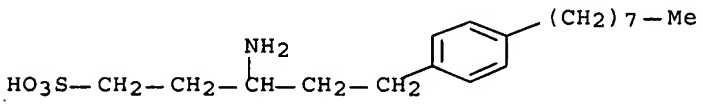
CRN 76-05-1
CMF C2 H F3 O2



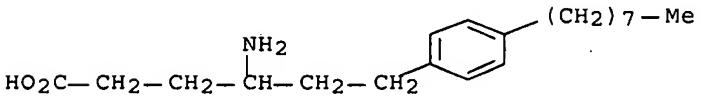
RN 596819-89-5 CAPLUS
CN Benzenebutanamide, .alpha.-amino-4-octyl-N-1H-tetrazol-5-yl-, monohydrochloride (9CI) (CA INDEX NAME)



RN 596819-90-8 CAPLUS
CN Benzenepentanesulfonic acid, .gamma.-amino-4-octyl- (9CI) (CA INDEX NAME)

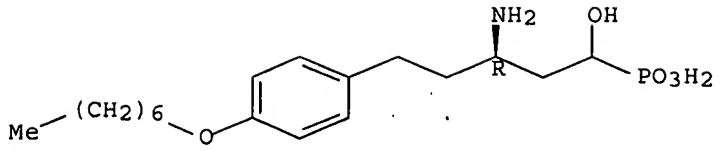


RN 596819-92-0 CAPLUS
CN Benzenehexanoic acid, .gamma.-amino-4-octyl- (9CI) (CA INDEX NAME)



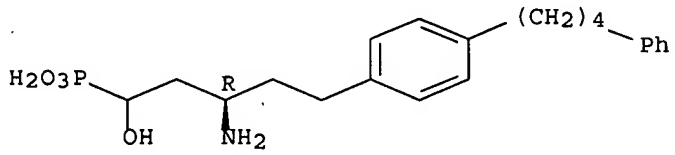
RN 596819-97-5 CAPLUS
CN Phosphonic acid, [(3R)-3-amino-5-[4-(heptyloxy)phenyl]-1-hydroxypentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



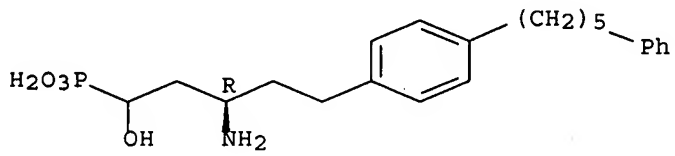
RN 596819-99-7 CAPLUS
CN Phosphonic acid, [(3R)-3-amino-1-hydroxy-5-[4-(4-phenylbutyl)phenyl]pentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



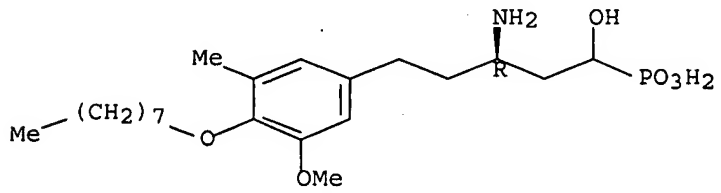
RN 596820-00-7 CAPLUS
CN Phosphonic acid, [(3R)-3-amino-1-hydroxy-5-[4-(5-phenylpentyl)phenyl]pentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



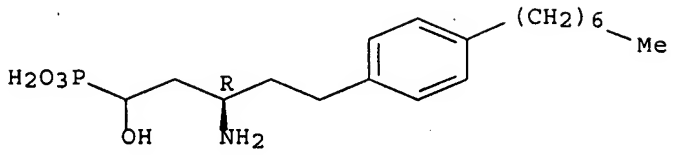
RN 596820-06-3 CAPLUS
CN Phosphonic acid, [(3R)-3-amino-1-hydroxy-5-[3-methoxy-5-methyl-4-(octyloxy)phenyl]pentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 596820-07-4 CAPLUS
CN Phosphonic acid, [(3R)-3-amino-5-(4-heptylphenyl)-1-hydroxypentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

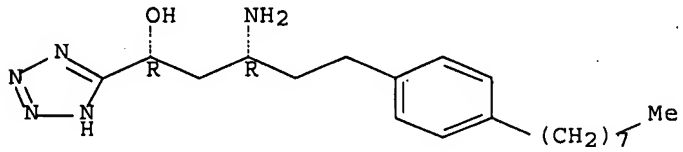


RN 597340-06-2 CAPLUS
CN 1H-Tetrazole-5-methanol, .alpha.-[(2R)-2-amino-4-(4-octylphenyl)butyl]-, (.alpha.R)-rel-, trifluoroacetate (salt) (9CI) (CA INDEX NAME)

CM 1

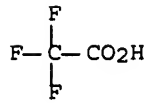
CRN 597340-05-1
CMF C20 H33 N5 O

Relative stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

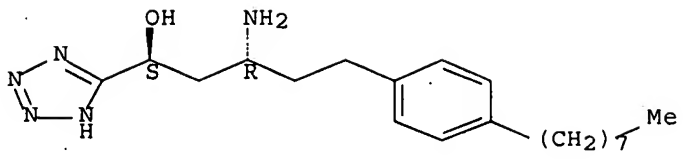


RN 597340-13-1 CAPLUS
CN 1H-Tetrazole-5-methanol, .alpha.-[(2R)-2-amino-4-(4-octylphenyl)butyl]-, (.alpha.S)-rel-, trifluoroacetate (salt) (9CI) (CA INDEX NAME)

CM 1

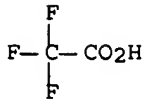
CRN 597340-12-0
CMF C20 H33 N5 O

Relative stereochemistry.



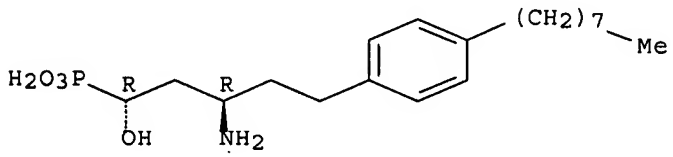
CM 2

CRN 76-05-1
CMF C2 H F3 O2



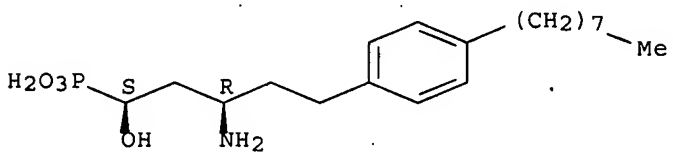
RN 597340-18-6 CAPLUS
CN Phosphonic acid, [(1R,3R)-3-amino-1-hydroxy-5-(4-octylphenyl)pentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



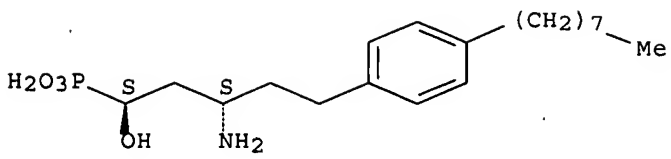
RN 597340-22-2 CAPLUS
CN Phosphonic acid, [(1S,3R)-3-amino-1-hydroxy-5-(4-octylphenyl)pentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



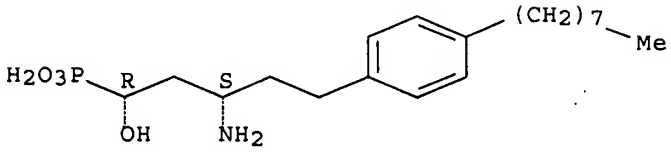
RN 597340-27-7 CAPLUS
CN Phosphonic acid, [(1S,3S)-3-amino-1-hydroxy-5-(4-octylphenyl)pentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

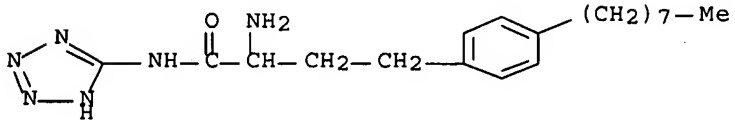


RN 597340-33-5 CAPLUS
CN Phosphonic acid, [(1R,3S)-3-amino-1-hydroxy-5-(4-octylphenyl)pentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 597342-93-3 CAPLUS
CN Benzenebutanamide, .alpha.-amino-4-octyl-N-1H-tetrazol-5-yl- (9CI) (CA INDEX NAME)



late

L11 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:478970 CAPLUS Full-text
DOCUMENT NUMBER: 138:49606
TITLE: The immune modulator FTY720 targets sphingosine 1-phosphate receptors
AUTHOR(S): Brinkmann, Volker; Davis, Michael D.; Heise, Christopher E.; Albert, Rainer; Cottens, Sylvain; Hof, Robert; Bruns, Christian; Prieschl, Eva; Baumruker, Thomas; Hiestand, Peter; Foster, Carolyn A.; Zollinger, Markus; Lynch, Kevin R.
CORPORATE SOURCE: Department of Transplantation, Novartis Pharma AG, Basel, CH-4002, Switz..
SOURCE: Journal of Biological Chemistry (2002), 277(24), 21453-21457
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

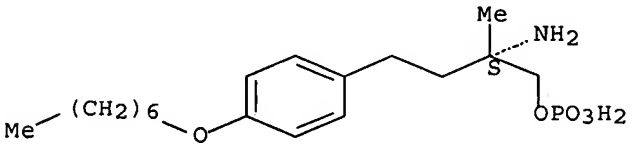
AB Immunosuppressant drugs such as cyclosporin have allowed widespread organ transplantation, but their utility remains limited by toxicities, and they are ineffective in chronic management of autoimmune diseases such as multiple sclerosis. In contrast, the immune modulating drug FTY720 is efficacious in a variety of transplant and autoimmune models without inducing a generalized immunosuppressed state and is effective in human kidney transplantation. FTY720 elicits a lymphopenia resulting from a reversible redistribution of lymphocytes from circulation to secondary lymphoid tissues by unknown mechanisms. Using FTY720 and several analogs, we show now that FTY720 is phosphorylated by sphingosine kinase; the phosphorylated compd. is a potent agonist at four sphingosine 1-phosphate receptors and represents the therapeutic principle in a rodent model of multiple sclerosis. Our results suggest that FTY720, after phosphorylation, acts through sphingosine 1-phosphate signaling pathways to modulate chemotactic responses and lymphocyte trafficking.

IT 479201-17-7
RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cimmunomodulators FTY720 and analogs target sphingosine 1-phosphate receptors)

RN 479201-17-7 CAPLUS

CN Benzenebutanol, .beta.-amino-4-(heptyloxy)-.beta.-methyl-, dihydrogen phosphate (ester), (.beta.S)- (9CI) (CA INDEX NAME)

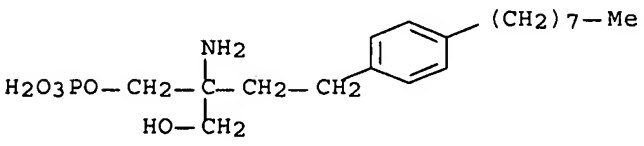
Absolute stereochemistry.



IT 402615-91-2 479201-16-6
RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(immunomodulators FTY720 and analogs target sphingosine 1-phosphate receptors)

RN 402615-91-2 CAPLUS

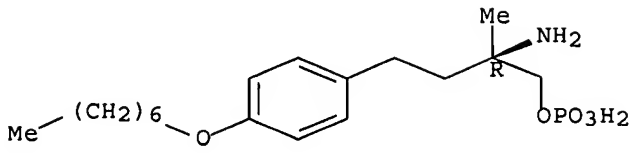
CN 1,3-Propanediol, 2-amino-2-[2-(4-octylphenyl)ethyl]-, 1-(dihydrogen phosphate) (CA INDEX NAME)



RN 479201-16-6 CAPLUS

CN Benzenebutanol, .beta.-amino-4-(heptyloxy)-.beta.-methyl-, dihydrogen phosphate (ester), (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

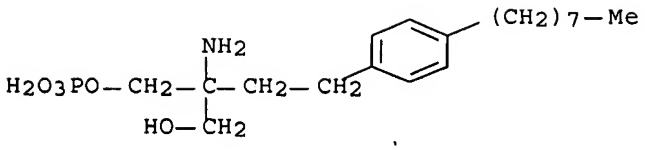
L11 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:301209 CAPLUS Full-text
DOCUMENT NUMBER: 137:241872
TITLE: Alteration of lymphocyte trafficking by sphingosine-1-phosphate receptor agonists
AUTHOR(S): Mandala, Suzanne; Hajdu, Richard; Bergstrom, James; Quackenbush, Elizabeth; Xie, Jenny; Milligan, James; Thornton, Rosemary; Shei, Gan-Ju; Card, Deborah; Keohane, Carolann; Rosenbach, Mark; Hale, Jeffrey; Lynch, Christopher L.; Rupprecht, Kathleen; Parsons, William; Rosen, Hugh
CORPORATE SOURCE: Departments of Immunology and Rheumatology, Merck Res. Laboratories, Rahway, NJ, 07065, USA
SOURCE: Science (Washington, DC, United States) (2002), 296(5566), 346-349
CODEN: SCIEAS; ISSN: 0036-8075
PUBLISHER: American Association for the Advancement of Science
DOCUMENT TYPE: Journal
LANGUAGE: English

4/12/2002

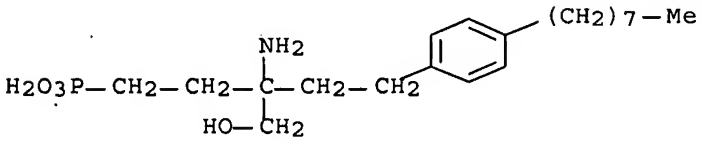
AB Blood lymphocyte nos., essential for the development of efficient immune responses, are maintained by recirculation through secondary Lymphoid organs. We show that lymphocyte trafficking is altered by the lysophospholipid sphingosine-1-phosphate (S1P) and by a phosphoryl metabolite of the immunosuppressive agent FTY720. Both species were high-affinity agonists of at least four of the five S1P receptors. These agonists produce lymphopenia in blood and thoracic duct lymph by sequestration of lymphocytes in lymph nodes, but not spleen. S1P receptor agonists induced emptying of lymphoid sinuses by retention of lymphocytes on the abluminal side of sinus-lining endothelium and inhibition of egress into lymph. Inhibition of lymphocyte recirculation by activation of S1P receptors may result in therapeutically useful immunosuppression.

IT 402615-91-2 402615-93-4
RL: PAC (Pharmacological activity); BIOL (Biological study)
(alteration of lymphocyte trafficking by sphingosine-1-phosphate receptor agonists)

RN 402615-91-2 CAPLUS
CN 1,3-Propanediol, 2-amino-2-[2-(4-octylphenyl)ethyl]-, 1-(dihydrogen phosphate) (CA INDEX NAME)



RN 402615-93-4 CAPLUS
CN Phosphonic acid, [3-amino-3-(hydroxymethyl)-5-(4-octylphenyl)pentyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=>

---Logging off of STN---

=>
Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	357.45	713.08

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-52.26	-52.26

STN INTERNATIONAL LOGOFF AT 07:28:45 ON 19 JUL 2007